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:	CROWNE PLAZA HOTEL 1177 AIRPORT BOULEVARD BURLINGAME, CALIFORNIA
DATE:	SEPTEMBER 5 AND 6, 2012 4 P.M. AND 9 A.M.
REPORTER:	BETH C. DRAIN, CSR CSR. NO. 7152
BRS FILE NO.:	91120 & 91121

I N D E X

I N D E X (CONT'D.)

BURLINGAME, CALIFORNIA; WEDNESDAY, SEPTEMBER 5, 2012

4 P.M.

CHAIRMAN THOMAS: GOOD AFTERNOON, EVERYBODY. I WOULD LIKE TO CALL THIS SEPTEMBER 5, 2012, MEETING OF THE INDEPENDENT CITIZENS OVERSIGHT COMMITTEE OF CIRM TO ORDER. MARIA, WOULD YOU PLEASE LEAD US IN THE PLEDGE OF ALLEGIANCE.

(THE PLEDGE OF ALLEGIANCE.)

CHAIRMAN THOMAS: BEFORE I TURN TO MARIA TO THE NEXT ITEM ON THE AGENDA, WHICH IS ROLL CALL, I WOULD LIKE TO PERSONALLY WELCOME OUR NEWEST MEMBER OF THE BOARD, DR. ANNE-MARIE DULIEGE, WHO JOINS US --

(APPLAUSE.)

CHAIRMAN THOMAS: -- FROM A LONG CAREER IN INDUSTRY, HAS GREAT EXPERTISE IN CLINICAL TRIALS, AND THE PROCESS OF GETTING DRUGS OR THERAPIES THROUGH THE FDA GAUNTLET, WHICH IS A SKILL THAT WILL BE INCREASINGLY CALLED UPON GOING FORWARD HERE AS WE PROCEED WITH OUR PROJECTS GETTING FURTHER AND FURTHER TOWARDS THE CLINIC. SO, DR. DULIEGE, WE'RE DELIGHTED TO HAVE YOU ABOARD AND ARE VERY HAPPY TO HAVE YOU HERE. SO THANK YOU VERY MUCH.

DR. DULIEGE: THANK YOU TO YOU, JON, AND

THANK YOU FOR THE ENTIRE COMMITTEE FOR WELCOMING ME. AND, INDEED, I LOOK FORWARD TO CONTRIBUTION GIVEN MY EXPERIENCE IN DRUG DEVELOPMENT AND AS A PEDIATRICIAN AS WELL. THANK YOU.

CHAIRMAN THOMAS: THANK YOU. MARIA, WILL YOU PLEASE CALL THE ROLL.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: HERE.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: HERE.

MS. BONNEVILLE: JACOB LEVIN.

DR. LEVIN: HERE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: HERE.

MS. BONNEVILLE: MARCY FEIT. MICHAEL FRIEDMAN.

DR. FRIEDMAN: HERE.

MS. BONNEVILLE: LEEZA GIBBONS.

MS. GIBBONS: HERE.

MS. BONNEVILLE: MICHAEL GOLDBERG. SAM HAWGOOD.

DR. HAWGOOD: HERE.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: HERE.

MS. BONNEVILLE: SHERRY LANSING. BERT

LUBIN.

DR. LUBIN: HERE.

MS. BONNEVILLE: MICHAEL MARLETTA. LEON FINE.

DR. FINE: HERE.

MS. BONNEVILLE: PHIL PIZZO. CLAIRE POMEROY.

DR. POMEROY: HERE.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. BONNEVILLE: CARMEN PULIAFITO.

DR. PULIAFITO: PRESENT.

MS. BONNEVILLE: ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.

MS. SAMUELSON: PRESENT.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: HERE.

MS. BONNEVILLE: JONATHAN SHESTACK.

MR. SHESTACK: HERE.

MS. BONNEVILLE: OSWALD STEWARD. JONATHAN THOMAS.

CHAIRMAN THOMAS: HERE.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: HERE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: HERE.

MS. BONNEVILLE: JAMES ECONOMOU.

CHAIRMAN THOMAS: THANK YOU, MARIA. WE'LL PROCEED NOW TO THE CHAIR'S REPORT. FIRST AND FOREMOST ON THAT, FOLLOWING ON THE INTRODUCTION OF DR. DULIEGE, I WOULD LIKE TO NOTE THAT OUR COLLEAGUE JEFF SHEEHY HAS BEEN REAPPOINTED AND OFFICIALLY SWORN IN FOR HIS NEXT TERM. AND WE'RE DELIGHTED TO HAVE THAT GOOD NEWS IN THE BANK AND LOOK FORWARD TO MANY MORE YEARS OF GREAT PARTICIPATION AND INPUT BY JEFF. SO, JEFF, CONGRATULATIONS.

MR. SHEEHY: THANK YOU.

CHAIRMAN THOMAS: I WOULD ALSO LIKE TO NOTE, AS YOU RECALL, DR. TED LOVE PREVIOUSLY HAD RESIGNED FROM THE BOARD. JOINING HIM IN RESIGNING IS DAVID SERRANO-SEWELL, WHO RECENTLY WAS APPOINTED -- ART, WOULD YOU LIKE TO SPEAK TO HIS APPOINTMENT FOR JUST A SECOND?

MR. TORRES: YES. HE WAS APPOINTED BY THE GOVERNOR LAST WEEK TO THE CALIFORNIA MEDICAL QUALITY ASSURANCE BOARD. AND I THINK IT'S A PERFECT LOCATION FOR DAVID, AND I THINK HE'S GOING TO CONTRIBUTE TREMENDOUSLY IN THAT AREA.

CHAIRMAN THOMAS: BOTH TED AND DAVID WILL BE HERE TOMORROW TO RECEIVE THEIR RESOLUTIONS AND

DUE PRAISE FOR ALL THE MANY YEARS OF GREAT SERVICE TO THE BOARD.

OVER THE PAST FEW WEEKS, AS YOU RECALL, OUR LAST MEETING WAS IN LATE JULY, OR ACTUALLY I STAND CORRECTED, OUR LAST IN-PERSON MEETING WAS LATE JULY. WE HAD A SUBSEQUENT BOARD MEETING DEALING WITH A COUPLE OF AGENDA ITEMS THAT WAS TELEPHONIC IN THE INTERIM, WHICH WERE ITEMS THAT WERE LEFT OVER FROM THE JULY AGENDA.

WE HAVE HAD ALSO A MOST RECENT MEETING OF THE CLINICAL DEVELOPMENT ADVISORY PANEL WHICH, AS YOU RECALL, EVALUATES PROGRESS REPORTS ON OUR FIRST ROUND OF DISEASE TEAMS. OBVIOUSLY WE'LL EVALUATE THE SECOND ROUND AS WELL DOWN THE ROAD, BUT THIS WAS THE LATEST INSTALLMENT OF THAT. WE HAD A NUMBER OF OUR DISEASE TEAMS PRESENTED. AND UNDER THE GUIDANCE OF DR. FEIGAL, AN EXPERT PANEL GAVE GREAT INPUT AND SUGGESTION TO THE PROJECTS AND PI'S WHO WERE THERE TO PRESENT THEM, AND I THINK CONTINUES TO BE A VERY VALUABLE EVALUATIVE TOOL WITH WHICH WE CAN MEASURE HOW OUR HARD-EARNED STATE DOLLARS ARE BEING UTILIZED TOWARDS THE PARTICULAR PROJECTS AND POTENTIAL THERAPIES AND CURES IN QUESTION. WE HAVE A COUPLE MORE IN THIS MOST RECENT SERIES OF THE CLINICAL DEVELOPMENT ADVISORY PANEL MEETINGS COMING UP IN THE

COMING WEEKS.

WE HAD OCCASION, MARIA AND I ACTUALLY ATTENDED A MEETING OF THE BIOTECH FOUNDATION IN CALIFORNIA ENDOWMENT, WHICH WAS DESIGNED TO SORT OF MEASURE WAYS TO IMPROVE THE LOT OF CALIFORNIA'S BIOTECH INDUSTRY AND WAYS TO ADVANCE THE CAUSE. THERE WERE MANY IN ATTENDANCE, AND WE HAD A VERY ROBUST DISCUSSION ON A LOT OF VERY INTERESTING TOPICS. AND I EXPECT THAT THERE WILL BE A REPORT GENERATED FROM THAT WHICH I WILL DISTRIBUTE IN DUE COURSE TO THE BOARD FOR ITS REVIEW.

SENATOR TORRES AND I HAD A GOOD BRIEFING MEETING WITH THE LIEUTENANT GOVERNOR WHERE WE BROUGHT HIM UP TO SPEED ON THE LATEST DEVELOPMENTS AT CIRM OVER THE PAST FEW MONTHS. AND I THINK, SENATOR, I CAN ACCURATELY CONVEY TO THE BOARD THAT THE LIEUTENANT GOVERNOR WAS VERY IMPRESSED WITH THE WORK THAT EVERYBODY IS DOING HERE AND DELIGHTED THAT PROGRESS IS BEING MADE ON A WHOLE HOST OF FRONTS.

IN ADDITION TO THAT, WE HAD A NUMBER OF NEW BOARD MEMBER OR ALTERNATE BOARD MEMBER BRIEFINGS WHICH WENT VERY WELL.

ON THE IOM FRONT, WE ARE, AS YOU KNOW, WELL INTO THE PROCESS OF THE IOM DOING A COMPREHENSIVE REVIEW OF CIRM. THEY ARE FINALIZING

ACTUALLY THE DRAFT REPORT WHICH IS NOW APPROACHING COMPLETION. WE EXPECT THAT THAT DRAFT WILL BE REVIEWED BOTH INTERNALLY AND EXTERNALLY OVER THE NEXT COUPLE OF MONTHS AND THAT WE WILL HAVE A FINAL REPORT READY TO BE DELIVERED, WE HOPE AND PLAN, TO THE BOARD BY A MEMBER OF THE IOM AT OUR DECEMBER 12TH BOARD MEETING IN LOS ANGELES.

I DO WANT TO MAKE NOTE ON THE BOARD MEETING, ON THE SUBJECT OF BOARD MEETINGS, OUR OCTOBER MEETING, WHICH WAS ORIGINALLY SCHEDULED IN IRVINE, IS NOW GOING TO BE UP HERE AGAIN. WE HAVE THE STRATEGIC PARTNERSHIP FUND, WHICH IS GOING TO BE DISCUSSED AT THAT MEETING, AND WE'VE DECIDED THAT SINCE SO MANY OF OUR HIGHLY CAPABLE STAFF NEED TO ATTEND MEETINGS IN WHICH WE'RE DISCUSSING OUR RFA'S AND THE PROJECTS, THAT IT'S BEST TO HAVE IT UP HERE TO SAVE MONEY. SO REGARDLESS OF WHAT YOUR CALENDARS MAY SAY, OCTOBER IN SAN FRANCISCO, WHICH, OF COURSE, IS A VERY NICE TIME OF YEAR.

SO WITH THAT, I THINK I WILL NOW TURN IT OVER TO DR. TROUNSON WHO WILL GIVE THE PRESIDENT'S REPORT, AND WE WILL PROCEED FORTHWITH THEREAFTER WITH ALL DELIBERATE SPEED TO THE REST OF THE AGENDA. DR. TROUNSON.

DR. TROUNSON: THANK YOU VERY MUCH, CHAIR.

I WON'T HOLD YOU UP TOO LONG FROM THAT IMPORTANT, INTERESTING DISCUSSION I'M SURE EVERYONE IS LOOKING FORWARD TO, BUT I WANTED TO SHARE WITH YOU A LITTLE BIT OF WORK ON THE HEART. I'VE JUST BEEN THROUGH AN EXERCISE MYSELF WHICH WAS EXTREMELY CHALLENGING. I SPENT FOUR OR FIVE DAYS IN THE BRAZILIAN SWAMPS, ALLIGATOR, CROCODILE INFESTED SWAMPS; BUT THEN I HAD ANOTHER FOUR DAYS IN LOS ANGELES AT DISNEYLAND AND UNIVERSAL STUDIOS. I CAN TELL YOU MY HEART STOOD UP TO EVERYTHING THAT WAS THROWN AT IT. CALIFORNIANS SCREAMING, EVERYBODY SCREAMING, FALLING DOWN 12 FLIGHTS IN THESE CRAZY HOTELS, MY HEART STOOD UP TO THIS REALLY WELL. AND I DIDN'T THINK IT COULD REALLY PUT UP. WHOEVER GOES ON THESE JAUNTS INTO THAT AREA, THAT'S A VERY WILD PLACE, LOS ANGELES. I'M GLAD I SURVIVED IT.

BUT I THOUGHT IN LIEU OF THE DISCUSSIONS THAT I OFTEN HAVE WITH YOU ABOUT THE WORK THAT'S UPCOMING, I WOULD CONCENTRATE ON THE HEART. I WASN'T SURE IF MINE WAS REALLY GOING TO TAKE CARE OF THAT IN BRAZIL AND LOS ANGELES, BUT IT SURVIVED IT.

SO I WANT TO BRING A FEW STUDIES HERE. AS I SAID, IT'S CONCENTRATING ON THE HEART. BUT THIS FIRST STUDY WAS PUBLISHED IN *SCIENCE TRANSLATIONAL MEDICINE*. AND IT'S A REALLY INTERESTING STUDY, I

THINK. IT INVOLVED THE SELF-ASSEMBLING NANOFIBERS THAT WERE PUT TOGETHER WITH VEG-F, WHICH IS A VASCULAR ENDOTHELIAL GROWTH FACTOR.

THESE SELF-ASSEMBLING FIBERS WERE INJECTED INTO TWO ANIMALS, RATS AND IN PIGS, AROUND THE BORDER ZONE OF A MYOCARDIAL INFARCT. WHEN THEY'D DONE THAT AND THEY LOOKED 28 DAYS LATER IN RATS, THEY SHOWED SIGNIFICANTLY IMPROVED CARDIAC FUNCTION THAT PREVENTED TISSUE REMODELING. THE TISSUE REMODELING IS A REALLY BAD PART OF MYOCARDIAL INFARCT. ALSO PREVENTED COLLAGEN DEPOSITION AND SCAR FORMATION, REDUCING THE INFARCT SIZE.

IN PIGS THEY HAD ALSO CONFIRMED THIS DATA. AND THE VEG-F WAS PROMOTING VERY STRONGLY ARTEROGENESIS, RECRUITING MYOFIBRILS AND CARDIOMYOCYTES TO THE DAMAGED MUSCLE. SO I THINK IT'S AN ENCOURAGING APPROACH USING A NANOTECHNOLOGY AND A GROWTH FACTOR THAT YOU COULD ACTUALLY USE TOGETHER WITH CELLS.

SO SHOWN ON THE LEFT-HAND SIDE IS WORK WITH THE RAT, AND ON THAT LEFT-HAND PANEL, IF YOU'RE LOOKING AT IT, NOT OVER YOUR SHOULDER, BUT IF YOU'RE LOOKING FORWARD, AND AT THE BOTTOM LEFT-HAND PANEL IS WHERE THEY'VE USED NANOFIBERS PLUS THE VEG-F. AND YOU CAN SEE THAT THE CARDIOMYOCYTES ARE THERE IN

MUCH MORE ROBUST FASHION. AND IF YOU LOOK AT THE PIG STUDIES, AGAIN, EVERY TIME YOU LOOK AT CARDIAC FUNCTION IN THESE ANIMALS, AND THE TOP ROW IS REALLY SHOWING YOU A MEASURE OF CARDIAC FUNCTION ON THE TOP ROW UNDER THE PIGS. STILL ON THE TOP ROW, BUT ON THE RIGHT-HAND SIDE IS SCAR SIZE. SO THE SCAR SIZE IS SMALLER. THE CARDIAC FUNCTION IS BETTER.

AND IF YOU LOOK AT CAPILLARY DENSITY ON THE BOTTOM, ON THE RIGHT-HAND SIDE OF EACH ONE OF THOSE GRAPHS AT THE BOTTOM UNDERNEATH THE PIG IS WHERE THEY USED THE COMBINED THERAPY. AND SO IN EACH SITUATION IT LOOKED IN BOTH ANIMALS LIKE VERY POSITIVE TO DO THIS. AND THIS IS SELF-ASSEMBLING GELS, VERY, VERY CLEVER. AND THEY INJECTED IT AND IT FORMS A GEL, BUT THOSE NANOFIBERS, THEY ACTUALLY FORM VERY TOUGH GEL FOR WHICH THEN ATTRACTS IN THESE CELLS AND ATTRACTS IN CELLS WHICH FORM CAPILLARIES AS WELL AS CELLS WHICH FORM CARDIOMYOCYTES.

THERE'S ALSO A SECOND STUDY THAT I PICKED OUT WHICH WAS IN *CELL STEM CELL*, AND IT'S WORK THAT WAS DONE AT SANFORD BURNHAM INSTITUTE WITH MARK, MERCOLA'S GROUP USING A SMALL MOLECULE, MEDIATED TGF-BETA-TYPE RECEPTOR DEGRADATION, WHICH PROMOTES CARDIOGENESIS IN EMBRYONIC STEM CELLS.

SO THE ESSAY WAS AN ES CELL ASSAY FOR

EXPRESSING THE MYO-GFP CARDIAC MARKER WHICH WAS USED IN HIGH THROUGHPUT SCREEN TO SMALL MOLECULE LIBRARY TO IDENTIFY A MOLECULE THAT IS AN INDUCER OF TYPE 2 TGF-BETA RECEPTOR DEGRADATION. SO THAT HAS THAT ITD 1. AND EFFECTIVELY CLEANS THE RECEPTOR FROM THE CELL SURFACE, WHICH SELECTIVELY INHIBITS CALCIUM SIGNALING. AND THEN IT SELECTIVELY ENHANCES THE DIFFERENTIATION OF ANY UNCOMMITTED MESODERM PROGENITORS INTO CARDIOMYOCYTES. IT'S A REALLY CLEVER CELL WHICH IS CLEANING OFF A RECEPTOR ON THE SURFACE THAT ALLOWS THE CELLS TO -- MORE OF THE CELLS IN YOUR POPULATION TO TURN TO CARDIOMYOCYTES. INSTEAD OF ONLY GETTING 25 OR 30 PERCENT CARDIOMYOCYTES, UP 60 PERCENT PLUS CARDIOMYOCYTES. SO A REALLY NEAT SMALL MOLECULE THAT COULD BE USED TO MAXIMIZE THE YIELD OF CARDIOMYOCYTES FROM HUMAN EMBRYONIC STEM CELLS.

THE THIRD STUDY WAS LOOKING AT ES CELL-DERIVED CARDIOMYOCYTES THAT ELECTRICALLY COUPLE AND SUPPRESS ARRHYTHMIAS IN INJURED HEART. NOW, THE BIG PROBLEM WITH ES CELL AND IPS CELL HUMAN CELLS, IF YOU DERIVED THEM AND PUT THEM INTO RODENTS, THE RODENT HEART IS BEATING THREE TIMES FASTER THAN THE HUMAN HEART, AND THEY REALLY CAN'T GET THERE. MY STAFF WERE AMAZED THAT MY HEART RATE COULD UP TO

TEN, AND THAT'S PROBABLY NOT A GOOD THING, BUT YOU CAN IN CULTURE GET HEART CELLS, HUMAN HEART CELLS, TO MOVE UP TO ABOUT 220, 230. WHILE YOU PROBABLY WOULDN'T RECOMMEND THAT FOR A LONG PERIOD OF TIME, YOU CAN -- THE GUINEA PIG OPERATES ITS HEART MUSCLE BEATING AT AROUND 200 TO 250, SO IT'S MUCH CLOSER TO THE HUMAN THAN THE RODENT. SO THEY USED A GUINEA PIG AS THE MODEL.

AND SO THEY WERE ABLE TO DEMONSTRATE IN THESE GUINEA PIGS, USING HUMAN EMBRYONIC STEM CELL-DERIVED CARDIOMYOCYTES, THAT THE ARRHYTHMIAS WERE PROTECTED, SO YOU DIDN'T GET ARRHYTHMIAS, AND YOU GOT THESE CELLS, THE HUMAN CELLS, BEATING SYNCHRONOUSLY WITH GUINEA PIG HEART CELLS. THIS IS THE FIRST TIME. THEY WON'T BEAT SYNCHRONOUSLY WITH RODENT CELLS. SO THIS LOOKS LIKE A BETTER MODEL. MAYBE IT WILL MAKE IT A SLOW GUINEA PIG TYPE OF ANIMAL, BUT THIS LOOKS LIKE IT WORKS REASONABLY WELL.

SO IMPROVED HEART MUSCLE FUNCTION AND SIGNIFICANTLY REDUCES SPONTANEOUSLY INDUCED TACHYCARDIA, IMPORTANT IN THESE ANIMALS. IN THE UNINJURED ANIMAL, THERE WAS A ONE-TO-ONE HOST-GRAFT CALCIUM-RELEASED COUPLING. AND IN THE INJURED HEARTS, THERE WAS HETEROGENEITY. YOU WOULD EXPECT

THAT BECAUSE SOME OF THE CELLS HAVE BEEN INJURED, SO THEY WOULDN'T ALL COUPLE UP CORRECTLY.

SO THIS SUPPORTS FURTHER EXPLORATION OF THE USE OF HUMAN EMBRYONIC STEM CELL-DERIVED CARDIOMYOCYTES IN MECHANICAL AND ELECTRICAL HEART REGENERATION IN THE HUMAN BECAUSE THERE'S BEEN SOME CONCERNS WHEN USING THE RODENT MODEL THAT IT REALLY WASN'T WORKING PROPERLY. AND I THINK YOU COULD SAY THAT IF YOU CHOOSE THE RIGHT MODEL, YOU CAN GET AN EFFECT.

AND THE LAST ONE I WANTED TO TALK TO YOU ABOUT WAS A COMPARISON OF HUMAN EMBRYONIC STEM CELLS WITH IPS CELLS BECAUSE THIS PAPER PROBABLY DOESN'T HAVE ENOUGH DATA TO BE TOTALLY CONVINCING, BUT I'LL SHOW YOU A COUPLE OF REALLY BRIEF VIDEOS WHICH WILL SHOW YOU THAT THERE'S REALLY QUITE A BIG DIFFERENCE.

SO THEY STUDIED TWO ES CELL LINES AND TWO IPS CELL LINES. NOT A LARGE NUMBER HERE. ALL THE CELL LINES EXPRESS CARDIOMYOCYTE LINKAGE MARKERS, ME, SP1, ILS1, AND NKX 2.5, CLASSICAL CARDIOMYOCYTE LINEAGE MARKERS. THE ES CELLS HAVE WIDESPREAD SARCOMERE STRIATIONS, WERE MULTILAYERED, AND SHOWED RHYTHMICAL CONTRACTION FOR UP TO A YEAR IN CULTURE. SO THAT'S A LONG TIME. IT'S A LONG TIME BEATING AWAY IN CULTURE.

AND THE IPS CELLS UNFORTUNATELY HAD A POORER INTERNAL DIFFERENTIATOR WITH FEW SARCOMERE STRIATIONS, WERE NOT MULTILAYERED, AND HAD SPORADIC CONTRACTILITY. SO IF I CAN GET THIS TO WORK NOW WITH A LITTLE LUCK HERE, THESE ARE THE HUMAN EMBRYONIC STEM CELLS BEATING IN THE MULTILAYERED FASHION THERE. AND, AGAIN, THIS IS AN EMBRYONIC STEM CELL-DERIVED CLUSTER THERE BEATING AWAY. SO YOU CAN SEE IT CAN BE QUITE ROBUST, AND THESE CELLS WILL GO ON FOR A VERY LONG TIME. THEY LOOK LIKE THEY PRODUCE LARGE NUMBERS OF THE CELLS REQUIRED, AND THEY LOOK PRETTY HEALTHY, BUT THESE ARE THE IPS CELLS.

I THINK, FIRST OF ALL, YOU CAN SEE THERE'S REALLY QUITE A DIFFERENCE IN THE STRUCTURES THERE. IT'S NOT MULTILAYERED. YOU CAN SEE THAT THE BEATS REALLY ARE SORT OF NOT AS THEY WERE IN THE ES CELLS. AND YOU CAN SEE THAT YOU GET DIFFERENT COLONIES BEATING AT DIFFERENT SITES. THERE'S ONE ON THE BOTTOM, AND THERE'S A COLONY UP THE TOP THERE BEATING AS WELL. SO THEY'RE QUITE INDEPENDENT OF ONE ANOTHER AND NOT IN SYNCHRONY. SO I THINK WITH IPS CELLS WE'VE STILL GOT A WAY TO GO TO MAKE THEM AS ROBUST AS EMBRYONIC STEM CELLS.

SO THOSE FEW PAPERS ATTRACTED MY ATTENTION

THIS TIME.

THE RFA PROGRAM, THE DISEASE TEAM THERAPY DEVELOPMENT, WE HOPE WE'LL COMPLETE THIS MEETING. RESEARCH LEADERSHIP THIS MEETING AS WELL. BASIC BIOLOGY IV, THE ICOC FUNDING DECISION THIS MEETING. SO GOT A LOT OF DECISIONS TO MAKE.

GENOMIC INITIATIVE, THE RFA WAS POSTED IN AUGUST AND THE WEBINAR ON SEPTEMBER 11TH. SO WE'RE GETTING CLOSE TO THAT. EARLY TRANSLATIONAL IV, THE RFA POSTING WILL BE IN SEPTEMBER. STRATEGIC PARTNERSHIP I AWARDS, THE GRANTS REVIEW OF APPLICATIONS WILL BE IN SEPTEMBER. WE WILL BE LOOKING AT -- THE GRANTS WORKING GROUP WILL BE LOOKING AT THE APPLICATIONS THAT ARE SUBMITTED. NEW FACULTY PHYSICIAN SCIENTIST TRANSLATIONAL RESEARCH AWARD, THEY'RE IN. GRANTS WORKING GROUP WILL REVIEW THOSE APPLICATIONS IN OCTOBER.

SO THERE'S A LOT OF WORK COMING UP ON ALL THE GRANTS WORKING GROUP. AND THEN, OF COURSE, THAT ALL HAS TO COME HERE. AND THE IPS CELL INITIATIVE, THE GRANTS WORKING GROUP WILL BE REVIEWING THOSE APPLICATIONS IN DECEMBER.

THERE HAVE BEEN A NUMBER OF MEETINGS AND WORKSHOPS HELD SINCE THE JULY ICOC MEETING, INCLUDING THE CREATIVITY AWARDS ANNUAL POSTER DAY.

UPCOMING, CIRM WEBINAR ON IMMUNE RESPONSE IN STEM CELL-BASED THERAPY. LEADING EXPERTS FROM FDA, INDUSTRY, ACADEMIA. THAT'S ON SEPTEMBER 27TH IF ANYBODY IS INTERESTED IN LISTENING IN. CIRM'S COLLABORATIVE FUNDING PARTNER WORKSHOP IN BRAZIL IN OCTOBER 1ST TO 2D IN SAO PAULO. SO THAT'S PRETTY WELL NOW ORGANIZED. CIRM-FDA ROUNDTABLE ON BEST PRACTICES IN CLINICAL DESIGN FOR FIRST-IN-HUMAN STEM CELL-BASED THERAPY IS ON OCTOBER 16TH IN ROCKVILLE.

CIRM'S ALPHA CLINICS WORKSHOP WILL BE ON NOVEMBER 14 TO 15 IN PALO ALTO. SO HOPEFULLY SOME OF THE PEOPLE WILL COME ALONG. I THINK JEFF HAS INDICATED AN INTEREST, BUT OTHERS, SO TOO ART. IT SHOULD BE REALLY, REALLY INTERESTING, I THINK.

CIRM GRANTEE MEETING MARCH NEXT YEAR, WE'RE GIVING PLENTY OF WARNING, 6TH TO THE 8TH. BEST STEM CELL MEETING IN THE WORLD STILL. THE CIRM-NIH PARKINSON'S DISEASE MEETING WILL BE IN MARCH NEXT YEAR.

THE CREATIVITY AWARDS HELD AT STANFORD, 65 SCIENTIFIC POSTERS PRESENTED BY HIGH SCHOOL INTERNS FROM NINE FUNDED CALIFORNIA INSTITUTIONS. THERE ARE FANTASTIC YOUNG PEOPLE THERE. 150 ATTENDEES, INCLUDING STUDENT INTERNS, PROGRAM DIRECTORS, PI'S, MENTORS, AND CIRM STAFF. IT WAS JUST A TERRIFIC

DAY. AND BEING AROUND THESE YOUNG STUDENTS AND THEIR POSTERS, THEY LOOK LIKE THEY WERE PH.D. STUDENTS TO ME, NOT HIGH SCHOOL INTERNS. THEY REALLY ARE FIRED UP. AND I THINK EACH OF THE UNIVERSITIES AND MEDICAL CENTERS THAT ARE WORKING WITH THESE STUDENTS, I THINK, HAVE DONE A FANTASTIC JOB ON THEM. SO THANK YOU VERY MUCH, ALL OF YOU, FOR LOOKING AFTER THESE KIDS. THEY LOVE IT. THEY LOVE THAT SUMMER PROGRAM.

AND THEY HAD KGO-TV SCIENCE REPORTER THERE WHO INTERVIEWED CIRM, MANI VESSAL, AND SELECTED STUDENTS FROM CHORI AND UCSF. THE STORY WILL BE ON AIR SHORTLY.

THE ALPHA CLINICS WORKSHOP, THE GOAL IS TO DEFINE WHAT CLINICAL CAPACITY IS NEEDED TO ACCELERATE DEVELOPMENT OF SAFE, EFFECTIVE, AND ACCESSIBLE CELL THERAPIES. PARTICIPANTS ARE GOING TO INCLUDE A RANGE OF STAKEHOLDERS, INVESTIGATORS FROM ACADEMIA AND INDUSTRY, CLINICAL TRIAL SPECIALISTS, CELL MANUFACTURERS, PATIENT ADVOCATES, REPRESENTATIVES FROM FUNDING AGENCIES, INSURERS, HEALTHCARE PROVIDERS, PHARMACEUTICAL INDUSTRY, AND INVESTORS. SO NATALIE DEWITT HAS BEEN BUSILY ARRANGING THIS, AND I THINK SHE'S GOT A PRETTY FULL PROGRAM FOR TWO DAYS WORKED OUT.

IN THE BUSINESS DEVELOPMENT, THE STRATEGIC PARTNERSHIP FUNDING RFA, THE FIRST ONE, IS UPCOMING AND WILL BE REVIEWED SEPTEMBER 12TH TO 14TH. SO WE'RE ALL LOOKING FORWARD TO THAT. IT WILL BE A LITTLE DIFFERENT BECAUSE THESE ARE ALL COMPANIES IN THIS PARTICULAR AWARD WHO ALL MADE IT THROUGH. STRONG INTEREST SHOWN BY INDUSTRY. WE ORIGINALLY HAD OVER 40 HANDS UP IN THIS. WE'VE COME DOWN, I THINK, TO 11 APPLICATIONS IN THE END.

A LONG-TERM FOCUS CONTEMPLATES REPLENISHMENT AND A NUMBER OF ROUNDS CONTINUING BECAUSE THERE'S A LOT OF INTEREST IN THIS PARTICULAR PROGRAM. THIS RFA IS A CORNERSTONE FOR CIRM'S INDUSTRY ENGAGEMENT INITIATIVES. AND I WANT TO THANK ELONA FOR SORT OF REALLY HEADING THIS OUT. SHE'S DONE A FANTASTIC JOB IN ACTUALLY GETTING IT ALTOGETHER. AND, OF COURSE, SUPPORT BY ALL THE REST OF THE SCIENCE STAFF, BUT ELONA REALLY SORT OF PUT HER HEART BEHIND THIS.

ON A COMMERCIALIZATION UPDATE, I THOUGHT YOU'D JUST BE INTERESTED THAT WE'VE BEEN TRACKING OR STARTED TO TRACT SPIN-OUTS ARISING IN WHOLE OR PART FROM CIRM FUNDING. AND THERE ARE EIGHT COMPANIES BEEN IDENTIFIED ALREADY. THERE ARE PROBABLY SOME OTHERS, AND WE'RE STILL CONTINUING TO ASSEMBLE THAT

INFORMATION, BUT THEY'RE SHOWN THERE.

SO THESE ARE COMPANIES THAT ARE SPUN OUT FROM THE ACTIVITIES THAT WE'VE BEEN DOING. I THOUGHT WE SHOULD BRING THAT TO YOUR ATTENTION BECAUSE SOMETIMES WE'RE ASKED, WELL, HOW MANY AND WHERE AND WHO. AND THESE ARE THE STARTUPS THAT ARE IN PLACE, AND SOME OF THOSE ARE REALLY MOVING VERY EFFECTIVELY IN THEIR DEVELOPMENT. SO I THINK WE'LL SEE A LOT MORE OF THESE MOVING THROUGH THE SPACE. SO WE'LL TRY AND KEEP ATTENTION ON THAT AND SEE IF WE CAN CONTINUE THE COLLECTION OF THE DATA BECAUSE WE HAVEN'T ALWAYS TRIED TO COLLECT THIS FROM THE BEGINNING, BUT WE THINK IT'S IMPORTANT TO HAVE THAT AND DEMONSTRATE THAT WE'RE ALSO INITIATING SOME OF THE START-UP COMPANIES.

I WANTED TO JUST GIVE YOU THE AWARDS FORECAST BECAUSE I NEED TO REMIND ALL OF US. IN THE BLUE IS WHAT WE'VE ACTUALLY ALREADY ALLOCATED. SO THE YEARS ARE SHOWN ACROSS THE BOTTOM THERE. SO THE ONE WITH THE GREEN BARS IS THE UNALLOCATED. SO THAT'S STILL FOR YOU TO ALLOCATE, BUT YOU NOTICE THE BLUE IS CONSIDERABLY MORE THAN THE GREEN. THE PURPLE IS THOSE ONES THAT YOU'VE AGREED TO, BUT WE REALLY HAVEN'T ADDED THE PROJECTS TO THEM YET, BUT THEY'VE BEEN AGREED TO AT THE BOARD, BUT WE'RE STILL

GOING THROUGH THE PROCESS OF AWARDING THE GRANTS.

SO I THINK THIS PERSPECTIVE YOU PROBABLY NEED TO KEEP SOME IDEA AS WE MOVE FORWARD BECAUSE YOU CAN SEE THE BLUE IS NOW STARTING TO DOMINATE. WE'RE GETTING A LITTLE BIT FURTHER THAN 50 PERCENT FORWARD NOW. SO THERE'S REALLY ONLY ABOUT 800, 900 MILLION THERE. IT'S GETTING SMALLER THAN THE 3 BILLION THAT WE HAD IN THE BEGINNING.

SO I THOUGHT IT'S IMPORTANT TO JUST KEEP TRACK OF THAT SO THAT YOU'VE GOT SOME IDEA WHERE WE ARE IN THE SPACE.

NOW, I THINK THE NEXT ONE I WANTED TO DO IS TO CALL ON CHILA. CHILA IS GOING TO PROVIDE YOU WITH THE FINANCE REPORT.

CHAIRMAN THOMAS: BEFORE CHILA SPEAKS, WE'D JUST LIKE THE BOARD TO KNOW THAT VERY RECENTLY CHILA HAS BEEN PROMOTED TO A POSITION OF DIRECTOR OF FINANCE. SO WELCOME OUR NEWEST DIRECTOR OF FINANCE TO GIVE THIS REPORT.

MS. SILVA-MARTIN: THANK YOU VERY MUCH. THANK YOU, DR. TROUNSON. GOOD AFTERNOON, MR. CHAIR, MEMBERS OF THE BOARD. I'M GOING TO GIVE YOU A BRIEF REPORT ON CIRM'S FINANCES. FIRST OF ALL, I WANT TO LET YOU KNOW THAT WE'VE COMPLETED THE 2011-12 FISCAL YEAR IN PROCESS. IT WAS A VERY SMOOTH PROCESS, AND

WE WERE ABLE TO SUCCESSFULLY SUBMIT OUR REPORT TO THE STATE CONTROLLER'S ON TIME.

SO NOW TO GIVE YOU A HIGH LEVEL COMPARISON OF OUR EXPENDITURES FROM THE 11-12 FISCAL YEAR TO 2010-11. OUR OPERATION EXPENSES TOTALED $15.4 MILLION IN 11-12 FISCAL YEAR AS COMPARED TO THE PRIOR YEAR, WHICH WAS 14.1. SO THERE WAS AN INCREASE OF $1.3 MILLION IN EXPENDITURES.

SIMILARLY, OUR GRANT PAYMENTS IN THE 11-12 FISCAL YEAR WERE $232 MILLION AS COMPARED TO THE PRIOR PERIOD, WHICH WAS $201 MILLION.

NOW LOOKING AT THE NEXT CHART, IT PROVIDES YOU WITH A COMPARISON OF OUR 2011-12 EXPENDITURES AGAINST THE BUDGET THAT WAS ALLOCATED. SO AS YOU CAN SEE ON THE CHART, WE WERE ALLOCATED A TOTAL OF $18.1 MILLION, AND OUR ACTUAL EXPENDITURES CAME IN AT 15.4 MILLION WITH A VARIANCE OF ABOUT $3 MILLION.

WE HAD SAVINGS IN ALL OF OUR EXPENDITURE CATEGORIES EXCEPT FOR ONE, AND THE MAJORITY OF THE SAVINGS WAS IN THREE CATEGORIES. IT WAS IN EMPLOYEE EXPENSES, IN CONTRACTING, AND IN GRANTS REVIEW. THE SAVINGS IN OUR EMPLOYEE EXPENSES WERE DUE IN LARGE PART TO VARIOUS VACANCIES THAT WE HAD THROUGHOUT THE YEAR AND THE ASSOCIATED BENEFITS WITH THOSE POSITIONS. SEVERAL VACANCIES DURING THE YEAR,

INCLUDING A MEDICAL OFFICER POSITION. AS YOU MAY RECALL, OUR DIRECTOR OF PUBLIC COMMUNICATIONS WAS VACANT FOR ABOUT NINE MONTHS. OUR I.T. DIRECTOR POSITION WAS VACANT TEN MONTHS. THE CHIEF FINANCE OFFICER POSITION WAS ALSO VACANT FOR ABOUT FIVE MONTHS. AND THEN THERE WAS A VARIETY OF OTHER POSITIONS THAT WERE VACANT ANYWHERE FROM TWO TO FOUR MONTHS, AND THAT REALLY RESULTED IN THE $1 MILLION SAVINGS.

WE ALSO HAD SAVINGS IN OUR CONTRACTING CATEGORY. AND THAT WAS REALLY A RESULT OF CONTRACTS THAT DID NOT MATERIALIZE OR THAT MATERIALIZED AT A LOWER LEVEL, SUCH AS OUR LEGAL SERVICES. AS YOU MAY RECALL, WE MADE AN EFFORT TO REDUCE OUR COSTS FOR OUR ANNUAL REPORT, SO WE HAD SAVINGS FROM THAT. WE HAD SAVINGS FROM A VARIETY OF OTHER CONTRACTS LIKE OUR VIDEO SPOTLIGHT SERVICES AND SOME OTHER SERVICES THAT DID NOT MATERIALIZE, LIKE THE CLUSTER ANALYSIS.

ANOTHER AREA WHERE WE HAD PRETTY SIGNIFICANT SAVINGS WAS IN THE GRANTS REVIEWS. SO FOR THE 11-12 FISCAL YEAR, WE HAD ACTUALLY BUDGETED FOUR CLINICAL DEVELOPMENT ADVISORY PANEL REVIEWS, AND WE ACTUALLY ONLY HELD THREE. AND EVEN FOR THE THREE THAT WE HELD, THE COST FOR THOSE CAME IN LOWER THAN WE HAD BUDGETED. AND THEN OUR COST FOR THE

VARIOUS GRANTS WORKING GROUP REVIEWS THAT WE HAD ALSO ALL CAME IN LOWER THAN WE BUDGETED.

SO THE SAVINGS WERE REALLY A RESULT OF THE GRANTS WORK REVIEW STAFF WORKING REALLY HARD TO MAINTAIN COST AT THE LOWEST POSSIBLE LEVEL, AND THEY DID A REALLY GOOD JOB IN THAT AREA.

THERE WAS ONE AREA WHERE WE ACTUALLY DID EXPEND A LITTLE BIT MORE THAN WAS BUDGETED. AS YOU MAY RECALL, FOR THE 11-12 FISCAL YEAR, OUR I.T. DIRECTOR WAS ACTUALLY BUDGETED IN EMPLOYEE EXPENSES. IN THE PREVIOUS YEAR WE HAD CONTRACTED FOR THOSE SERVICES; HOWEVER, BECAUSE WE DID NOT FILL THE POSITION FOR THE I.T. DIRECTOR UNTIL MAY OF THIS YEAR, WE CONTINUED TO SECURE THE I.T. DIRECTOR SERVICES THROUGH A CONTRACT. SO IT REALLY RESULTED IN AN OVERAGE IN OUR I.T. CATEGORY WITH THE CORRESPONDING SAVINGS IN OUR EMPLOYEE EXPENSES.

SO THEN THE NEXT SLIDE JUST GIVES YOU A REAL QUICK COMPARISON OF OUR VARIOUS COSTS AS COMPARED TO THE PREVIOUS YEAR. AND AS YOU CAN SEE, WE DO HAVE SOME VARIANCES. AGAIN, THE BIGGEST VARIANCE IS IN EMPLOYEE EXPENSES, AND THAT WAS REALLY DUE TO OUR INCREASED STAFF LEVEL. WE WENT FROM 46 POSITIONS IN THE 2010-11 FISCAL YEAR TO 54 POSITIONS IN THE 11-12 FISCAL YEAR. WE ALSO HAD

MERIT ADJUSTMENTS IN THIS FISCAL YEAR. OUR SCIENCE MEETINGS ARE HIGHER, AND IT WAS DUE TO THE WORLD STEM CELL SCHOLARSHIPS THAT WE GAVE OUT THIS YEAR, AS WELL AS THE GRANTEE MEETING THAT WE HOLD EVERY 18 MONTHS.

WE DID HAVE A LITTLE BIT OF SAVINGS IN OUR TRAVEL BUDGET, AND THAT WAS DUE TO AN INTERNAL FREEZE THAT WAS IMPOSED. AS YOU MAY RECALL, THE GOVERNOR ISSUED A DIRECTIVE FOR OUT-OF-STATE TRAVEL TO BE REDUCED. ALTHOUGH IT DID NOT APPLY TO US, THE DIRECTIVE, IT WAS DECIDED THAT WE WOULD PARTICIPATE. AND SO, THEREFORE, WE HAD SOME SAVINGS IN TRAVEL.

SO NOW ON TO THE CURRENT YEAR. I JUST WANT TO LET YOU KNOW THAT OUR 2011-12 ANNUAL FINANCIAL AUDIT IS UNDER WAY. IT'S BEING CONDUCTED BY MACIAS & GINI. AND THEN LET'S SEE. OUR AVAILABLE BOND CASH AS OF JULY 31ST IS 104.6 MILLION, WHICH IS ACTUALLY AN INCREASE OF 53.7 MILLION FROM JUNE 30TH. AND REALLY THE INCREASE IS DUE TO A RESULT OF THE COMMERCIAL PAPER THAT WE RECEIVED IN JULY.

AND THEN, FINALLY, I JUST WANT TO REPORT THAT WE WILL PROVIDE YOU WITH A FINANCIAL STATUS FOR 12-13 AT OUR NEXT ICOC BOARD MEETING. THAT CONCLUDES MY PRESENTATION. ARE THERE ANY QUESTIONS?

THANK YOU.

CHAIRMAN THOMAS: THANK YOU, CHILA. DR. TROUNSON, DOES THAT CONCLUDE YOUR REPORT?

DR. TROUNSON: YES, IT DOES.

CHAIRMAN THOMAS: THANK YOU VERY MUCH. OKAY. WE'LL NOW PROCEED -- ACTUALLY BEFORE WE PROCEED, LET ME JUST -- TO MANAGE BOARD EXPECTATIONS ABOUT HOW THE MEETING HOPEFULLY WILL PROCEED HERE, WE HAVE A LOT OF THINGS TO GET THROUGH. IT IS MY GOAL TO GET THROUGH AS MUCH AS WE CAN TODAY SINCE EVERYBODY IS SORT OF HERE UNTIL LATER IN THE EVENING, AND TO LEAVE FOR TOMORROW ON THE AGENDA ONLY THE BASIC BIO AWARDS, THE RESEARCH LEADERSHIP AWARD, THE SPOTLIGHT, WHICH WILL BE AT LUNCH, AND THE RESOLUTIONS FOR OUR PAST BOARD MEMBERS. EVERYTHING ELSE YOU SEE ON YOUR AGENDA I'M GOING TO TRY TO GET THROUGH TODAY. SO I WOULD ASK EVERYBODY TO BE AWARE OF THAT AND TO PROCEED ACCORDINGLY AS WE MOVE THROUGH THE VARIOUS TOPICS FOR DISCUSSION.

SO WE WILL START NOW WITH ACTION ITEM NO. 6, CONSIDERATION OF APPOINTMENT OF NEW SCIENTIFIC MEMBERS OF THE GRANTS WORKING GROUP. DR. SAMBRANO.

DR. SAMBRANO: THANK YOU, MR. CHAIRMAN, MEMBERS OF THE BOARD, MEMBERS OF THE PUBLIC. TODAY WE'RE BRINGING FOR YOUR CONSIDERATION TWO NOMINEES

FOR GRANTS WORKING GROUP MEMBERS THAT ARE BRINGING KEY SCIENTIFIC EXPERTISE IN THE AREA OF TISSUE ENGINEERING, MORE SPECIFICALLY RELATED TO TISSUE ENGINEERING IN CARDIOVASCULAR AND EYE CONDITIONS.

THE NOMINEES ARE SHOWN IN YOUR TAB 6. THEY ARE DR. CHRISTOPHER BREUER AND DR. MAY GRIFFITH. SO WE ARE SEEKING YOUR APPROVAL AND APPOINTMENT OF THESE NOMINEES AS MEMBERS OF THE WORKING GROUP.

CHAIRMAN THOMAS: DO I HEAR A MOTION TO THAT EFFECT?

DR. HAWGOOD: SO MOVED.

CHAIRMAN THOMAS: MOVED BY DEAN HAWGOOD. SECOND?

DR. POMEROY: SECOND.

CHAIRMAN THOMAS: DEAN POMEROY. ANY DISCUSSION BY MEMBERS OF THE BOARD? JAMES, IS THIS SOMETHING WE HAVE PUBLIC COMMENT ON IF THERE IS ANY?

MR. HARRISON: YES.

CHAIRMAN THOMAS: HEARING NO FURTHER BOARD DISCUSSION, ANY COMMENTS BY MEMBERS OF THE PUBLIC? HEARING NONE, I DON'T BELIEVE WE NEED A ROLL CALL, DO WE?

MR. HARRISON: JUST FOR MEMBER FEIT WHO'S ON THE TELEPHONE.

CHAIRMAN THOMAS: SO EVERYBODY IN THE ROOM APPROVING OF THIS MOTION PLEASE SIGNIFY BY SAYING AYE. OPPOSED? ABSTENTIONS? MARCY.

MS. FEIT: YES.

CHAIRMAN THOMAS: UNANIMOUSLY APPROVED. THANK YOU VERY MUCH.

ON TO ITEM NO. 7, CONSIDERATION OF AMENDMENTS TO THE GRANTS ADMINISTRATION POLICY. AMY, PLEASE PROCEED.

MS. LEWIS: THANK YOU, MR. CHAIRMAN. GOOD AFTERNOON, MEMBERS OF THE BOARD AND MEMBERS OF THE PUBLIC. WE'RE ON ITEM NO. 7 IN YOUR BINDERS. AND I'D LIKE TO REFER YOU TO THE MEMO THAT'S IN YOUR BINDERS AND THE ATTACHED CURRENT REDLINE VERSION OF THE GRANTS ADMINISTRATION POLICY FOR ACADEMIC AND NON-PROFIT INSTITUTIONS, WHICH INCLUDES ALL OF THE PROPOSED POLICY AMENDMENTS. I'M GOING TO WALK THROUGH THOSE BRIEFLY WITH YOU.

AS A REMINDER, THIS POLICY, WHICH WE COMMONLY REFER TO AS THE GAP, PROVIDES ALL OF THE DETAILED RULES REGARDING USE OF CIRM GRANT FUNDS. OUR GAP IS GENERALLY MODELED ON NIH'S GRANTS POLICY STATEMENT.

CIRM'S GAP HAS BEEN IN EFFECT SINCE 2006, AND WE MADE ONE ROUND OF AMENDMENTS TO THE POLICY IN

2009. TO INITIATE THIS CURRENT ROUND OF AMENDMENTS, WE CAME TO THE BOARD IN DECEMBER 2011 FOR APPROVAL TO OPEN THE PROCESS FOR ANOTHER ROUND OF REVISIONS TO THE GAP. SINCE THEN, WE'VE HAD TWO OPEN PUBLIC COMMENT PERIODS DURING WHICH WE SOLICITED COMMENTS FROM GRANTEES AND MEMBERS OF THE PUBLIC ON THE PROPOSED POLICY CHANGES. WE ALSO HELD AN INTERESTED PERSONS MEETING IN MARCH OF THIS YEAR TO GATHER ADDITIONAL COMMENTS.

IN THE GRANTS MANAGEMENT OFFICE, WE WORK WITH OUR GRANTEES EVERY DAY, AND WE BELIEVE THAT OUR GRANTEES WORK VERY HARD TO COMPLY WITH OUR POLICIES. IN COMMUNICATION WITH THEM, THEY PROVIDED US WITH FEEDBACK ABOUT APPLYING OUR REGULATIONS TO THEIR ACTIVE GRANTS AND ALSO WITH QUESTIONS ABOUT ALLOWABLE ACTIVITIES UNDER CIRM-FUNDED AWARDS. THIS HAS ALLOWED US TO IDENTIFY POINTS OF CONFUSION THAT MIGHT BE CLEARED UP BY STREAMLINING OR CLARIFYING THE LANGUAGE IN THE GAP.

WE'VE ALSO IDENTIFIED SOME ITEMS IN THE REGULATIONS THAT ARE REASONABLE AS WRITTEN, BUT HAVE CREATED UNINTENTIONAL ADMINISTRATIVE BURDEN ON OUR GRANTEES WITH NO CORRESPONDING BENEFIT TO CIRM'S MISSION.

SOME OF THE AMENDMENTS THAT WE'RE

PROPOSING ALSO REFLECT THE INCREASED CAPABILITIES OF OUR ONLINE GRANTS MANAGEMENT PORTAL WHICH HAS REDUCED THE NEED FOR PAPER AND PDF REPORT FORMS AND ALLOWED FOR MORE STREAMLINED REPORTING.

SO I'D LIKE TO QUICKLY MENTION A FEW OF THE SUBSTANTIVE CHANGES THAT WE'RE PROPOSING. FIRST, WE PROPOSE THE ADDITION OF SEVERAL NEW DEFINITIONS. THOSE ARE REALLY MADE NECESSARY BY THE LARGER, MORE COMPLEX AWARD THAT WE'RE FUNDING. SO WE PROPOSE TO INCLUDE DEFINITIONS FOR CO-PRINCIPAL INVESTIGATOR, MILESTONES, SUBAWARD, SUBRECIPIENT, FINANCIAL REPORT, AND WORKING BUDGET. THOSE WILL ALL BECOME DEFINED TERMS IN THE GAP.

AS DIRECTED BY THE STATE TREASURER'S OFFICE AND AFTER DISCUSSION WITH THE UC OFFICE OF THE PRESIDENT, WE ARE ALSO PROPOSING AN AMENDMENT TO PROVIDE FOR FLEXIBILITY TO MAKE PAYMENTS TO THE UC CAMPUSES ON A REIMBURSEMENT BASIS IN ORDER TO COMPLY WITH THE REQUIREMENTS OF TAX-EXEMPT BOND PROCEEDS -- OF USING TAX-EXEMPT BOND PROCEEDS.

THIS LANGUAGE PROVIDES FOR NEGOTIATION WITH INDIVIDUAL CAMPUSES TO ENSURE THAT PAYMENT SCHEDULES DO NOT CREATE UNDUE FINANCIAL CONSTRAINTS WITH GRANTEES.

SO AS I MENTIONED, WE'RE FUNDING LARGER,

MORE COMPLEX AWARDS LIKE THE DISEASE TEAM AWARDS THAT YOU'RE CONSIDERING AT THIS MEETING. THIS HAS REALLY REQUIRED US TO RECONSIDER SOME OF WHAT WE CALL PRIOR APPROVAL REQUIREMENTS. THIS IS WHEN A GRANTEE WANTS TO MAKE CHANGES UNDER THEIR AWARD AND THEY NEED PRIOR APPROVAL FROM CIRM TO DO SO.

SOME OF THE PROVISIONS IN THE GAP THAT WORKED QUITE WELL FOR THE SMALL AWARDS THAT WERE FUNDED IN THE BEGINNING SIMPLY DID NOT SCALE UP TO LARGE GRANTS WITH MULTIPLE RESEARCH COLLABORATIONS. SO THE AMENDMENTS THAT WE'RE PROPOSING IN THE PRIOR APPROVAL REQUEST SECTION WILL IMPROVE OUR ABILITY TO ADMINISTER THESE LARGER AWARDS.

ONE EXAMPLE IS THAT WE WILL REQUIRE SCIENCE OFFICE REVIEW BEFORE SUBSTANTIAL UNSPENT FUNDS CAN BE CARRIED FORWARD FROM ONE BUDGET PERIOD TO THE NEXT. THE THRESHOLD CHANGE HERE IS FROM A STRAIGHT 25-PERCENT CARRY-FORWARD ALLOWANCE TO THE LESSER OF 200,000 OR 25-PERCENT CARRY-FORWARD ALLOWANCE. AND AS YOU CAN IMAGINE, THAT MAKES A BIG DIFFERENCE IN SOME OF THESE LARGER $20 MILLION AWARDS.

SO FINALLY, WE'RE PROPOSING SEVERAL CHANGES THAT ARE SPECIFIC TO TRAINING GRANTS. FOR EXAMPLE, WE'RE PROPOSING SOME LANGUAGE THAT

CLARIFIES THAT GRANTEE INSTITUTIONS CAN APPLY THEIR OWN EXISTING INSTITUTIONAL POLICIES FOR TRAINEES TAKING PARENTAL LEAVE. WE'RE ALSO PROPOSING TO PUT A CAP ON THE NUMBER OF TRAINEES THAT CAN BE SUPERVISED BY A SINGLE MENTOR. THAT WOULD BE TWO CONCURRENT.

SO THAT'S A QUICK OVERVIEW OF THE MAJOR CHANGES THAT WE PROPOSE. MOST OF THE OTHER ITEMS THAT YOU WILL SEE, IF YOU LEAF THROUGH THAT POLICY, ARE REALLY MINOR HOUSEKEEPING ITEMS. I KNOW I WENT THROUGH THAT VERY QUICKLY. ARE THERE ANY QUESTIONS ABOUT THE ITEMS THAT I PRESENTED OR ANY OTHER ITEMS THAT YOU'VE SEEN IN THE POLICY? ANY QUESTIONS ABOUT THE PROCESS ITSELF?

SO I'M REQUESTING, I'D LIKE TO REQUEST THAT THE ICOC CONSIDER ADOPTING THE PROPOSED AMENDMENTS TO THE GAP AND PROCEED WITH FINALIZING THE PROCESS WITH THE OFFICE OF ADMINISTRATION LAW. WE'RE HOPING THAT THESE AMENDMENTS CAN TAKE EFFECT BEFORE WE INITIATE THE DISEASE TEAM AWARDS THAT YOU ARE CONSIDERING TODAY.

MR. TORRES: SO MOVED.

CHAIRMAN THOMAS: MOVED BY SENATOR TORRES.

DR. VUORI: SECOND.

CHAIRMAN THOMAS: SECOND BY DR. VUORI.

BEFORE WE GET YOUR VOTE, I'D JUST LIKE TO THANK AMY AND EVERYBODY IN GRANTS MANAGEMENT. THIS WAS DESCRIBED RATHER QUICKLY, BUT WAS THE PRODUCT OF A LOT OF WORK AND CONSIDERATION BY A LOT OF PEOPLE IN OUR CONTINUING EFFORTS TO UPDATE OUR PRACTICES TO BEST SERVE OUR MISSION. SO, AMY, THANK YOU VERY MUCH.

MR. TORRES: HERE. HERE. IT'S A REMARKABLE TEAM. YOUR LEADERSHIP HAS JUST BEEN TERRIFIC. NICE TO WORK YOU.

MS. LEWIS: THANK YOU.

CHAIRMAN THOMAS: ARE THERE COMMENTS BY MEMBERS OF THE BOARD ON THE MOTION? HEARING NONE, ANY COMMENTS BY MEMBERS OF THE PUBLIC? WE WILL THEN PROCEED TO A VOTE. AGAIN, THIS IS A VOICE VOTE ITEM. SO THOSE IN THE ROOM WHO APPROVE PLEASE SIGNIFY BY SAYING AYE. OPPOSED? ABSTAINING? MARCY.

MS. FEIT: YES.

CHAIRMAN THOMAS: UNANIMOUSLY APPROVED. THANK YOU VERY MUCH, AMY.

OKAY. WE ARE NOW GOING TO MOVE ON TO DISCUSSION OF OUR REMAINING PENDING DISEASE TEAM AWARDS. BEFORE WE GET INTO THAT, I JUST WANTED TO SAY A COUPLE THINGS. AT OUR LAST MEETING, AS YOU

RECALL, WE HAD A NUMBER OF EXTRAORDINARY PETITIONS. AND THE PROCESS THAT WE SETTLED ON AT THAT MEETING WAS, INSTEAD OF TRYING TO MAKE AN INSTANTANEOUS DECISION ON THE VIABILITY OF THE ADDITIONAL OR NEW INFORMATION PROVIDED BY THE APPLICANTS, WE FELT THAT IT WOULD BE BEST TO SEND THOSE THAT WERE SO REQUESTED BACK TO THE GRANTS WORKING GROUP FOR A RE-REVIEW OF VERY NARROW QUESTIONS THAT WERE RAISED DURING THE COURSE OF OUR DISCUSSION WITH THE DIRECTIVE TO THE GRANTS WORKING GROUP TO DETERMINE TO THE BEST OF THEIR ABILITY IF THE ADDITIONAL OR NEW OR CLARIFYING INFORMATION WOULD HAVE RESULTED IN A DIFFERENT RECOMMENDATION BY THE GRANTS WORKING GROUP FOR THE PROPOSALS IN QUESTION.

THAT PROCEDURE AT THE MEETING WE DIRECTED TO BE DETERMINED IN DETAIL BY DR. TROUNSON AND MR. SHEEHY, WHO MET AND SUBSEQUENTLY IN A MEETING I WAS ALSO ATTENDING DETERMINED THAT THE RE-REVIEWS WOULD BE DONE BY THE CHAIR OF THE GRANTS WORKING GROUP FOR THE DISEASE TEAM MEETING, ONE OF THE PRINCIPAL REVIEWERS OF THE PROPOSAL IN QUESTION, AND A PATIENT ADVOCATE.

THOSE RE-REVIEWS WERE DONE A WEEK AGO FRIDAY, JAMES, AND ARE NOW COMING BACK FOR DISCUSSION HERE AT THE BOARD MEETING. THERE WAS A

SIXTH EXTRAORDINARY PETITION WHICH WAS PUT OUT BY DR. LIPTON. THERE'S ADDITIONAL INFORMATION HE PROVIDED THAT WE'RE STILL WORKING ON EVALUATING. SO THAT PARTICULAR PROPOSAL WILL NOT BE DISCUSSED BY THE BOARD AT THIS MEETING AND IS BEING TABLED FOR REVIEW AND DISCUSSION AT THE OCTOBER MEETING.

SO HAVING SAID THAT, I'D LIKE TO JUST TURN IT OVER TO JAMES FOR FURTHER COMMENT ON THE PROCESS AND WHAT WE'RE GOING TO DO HERE AT THE BOARD MEETING GOING FORWARD WITH RESPECT TO THE FIVE PROPOSALS THAT WERE SENT BACK FOR RE-REVIEW.

MR. HARRISON: THANK YOU, J.T. AS J.T. EXPLAINED, AT THE LAST MEETING THE BOARD APPROVED EIGHT OF THE DISEASE TEAM APPLICATIONS, REFERRED FIVE OF THEM FOR ADDITIONAL ANALYSIS, AND DID NOT TAKE ACTION WITH RESPECT TO THE REMAINING APPLICATIONS IN TIER III.

IN ORDER TO TRY TO MAINTAIN AS ORDERLY AND EFFICIENT A PROCESS AS POSSIBLE, WHAT WE PLAN TO DO AFTER THE STAFF PRESENTATION IS TO FIRST TAKE UP THE FIVE APPLICATIONS THAT WERE THE SUBJECT OF THE ADDITIONAL ANALYSIS. AND WE PROPOSE TO START WITH THE THREE APPLICATIONS THAT WERE RECOMMENDED FOR FUNDING AND OPEN THE FLOOR FOR BOARD DISCUSSION OF THOSE APPLICATIONS AS WELL AS MOTIONS TO FUND THEM

ONE BY ONE IF A BOARD MEMBER SO DESIRES.

TO THE EXTENT ANY OF THE DISCUSSION WOULD REQUIRE STAFF TO PROVIDE PROPRIETARY INFORMATION, WE'LL DEFER CONSIDERATION OF THAT APPLICATION UNTIL AFTER WE'VE HAD AN OPPORTUNITY FOR A CLOSED SESSION.

AFTER WE'VE CONSIDERED THOSE THREE APPLICATIONS, WE'LL NEXT MOVE ON TO THE OTHER TWO APPLICATIONS THAT WERE THE SUBJECT OF ADDITIONAL ANALYSIS AND THAT WERE NOT RECOMMENDED FOR FUNDING. TO THE EXTENT THAT A BOARD MEMBER IS INTERESTED IN MAKING A MOTION OR DISCUSSING ONE OF THOSE APPLICATIONS, WE'LL OPEN THE FLOOR TO THAT DISCUSSION. AGAIN, IF THERE IS PROPRIETARY INFORMATION CONCERNING ONE OR MORE OF THE APPLICATIONS THAT THE BOARD NEEDS TO EVALUATE BEFORE MAKING A FINAL DECISION, WE'LL DEFER CONSIDERATION OF THAT APPLICATION OR APPLICATIONS UNTIL AFTER WE'VE CONVENED IN CLOSED SESSION.

AFTER WE'VE COMPLETED OUR DISCUSSION OF THOSE FIVE APPLICATIONS, WE'LL MOVE ON TO THE APPLICATIONS THAT REMAIN IN TIER III AND OPEN THE FLOOR TO DISCUSSION BY THE BOARD OF THOSE APPLICATIONS. AGAIN, ANY QUESTIONS THAT WOULD REQUIRE DISCUSSION OF PROPRIETARY INFORMATION, WE'LL DEFER CONSIDERATION OF THAT PARTICULAR APPLICATION

UNTIL AFTER CLOSED SESSION.

ONCE WE'VE HANDLED EVERYTHING WE CAN HANDLE IN OPEN SESSION, WE'LL CONVENE IN CLOSED SESSION, AND THEN RETURN TO OPEN SESSION AND TAKE ANY FINAL ACTION THAT'S NECESSARY, INCLUDING CLOSING FUNDING ON THE APPLICATIONS THAT REMAIN IN TIER III.

CHAIRMAN THOMAS: OKAY. THANK YOU.

MR. SHESTACK: THAT LEAVES US THREE OPPORTUNITIES FOR CLOSED SESSION?

MR. HARRISON: NO. WE'LL HAVE ONLY A SINGLE CLOSED SESSION, BUT WE'RE TALKING ABOUT THE APPLICATIONS IN THREE SEPARATE GROUPS. AND TO THE EXTENT THAT ANY PROPRIETARY INFORMATION IS IDENTIFIED WITH RESPECT TO AN APPLICATION IN ONE OF THOSE THREE GROUPS, WE'LL TABLE THAT DISCUSSION.

MR. SHESTACK: AND WE'LL HAVE ONE. OKAY. GREAT. THANK YOU VERY MUCH.

CHAIRMAN THOMAS: THANK YOU, JAMES. SO WHAT WE'RE GOING TO DO IS TO START OUT BY TAKING THE FIRST THREE PROJECTS THAT WERE -- DR. FEIGAL. I MISSED YOUR POWERPOINT UP THERE. IF YOU COULD GIVE AN OVERVIEW, AND THEN WE'LL PROCEED TO THE THREE THAT WERE RECOMMENDED FOR FUNDING.

DR. FEIGAL: THANK YOU VERY MUCH. SO I'M PLEASED TODAY TO PRESENT THE ADDITIONAL ANALYSIS

RESULTS ON THE DISEASE TEAM THERAPY DEVELOPMENT RESEARCH AWARDS. WHAT I'D LIKE TO DO, JUST TO SET THE CONTEXT, IS REMIND YOU WHAT THIS INITIATIVE WAS ABOUT: TO PROVIDE YOU A RECAP OF THE DECISIONS THAT TOOK PLACE AT THE JULY ICOC, TO DESCRIBE THE ADDITIONAL ANALYSIS PROCESS IN A LITTLE BIT MORE DETAIL, AND THEN TO PROVIDE THE RESULTS OF THE ADDITIONAL ANALYSIS DISCUSSION.

SO THIS RFA, 10-05, IS BASICALLY REALLY FOCUSED ON CIRM'S CLINICAL OBJECTIVE MISSION, WHICH IS TO ADVANCE THE STEM CELL-BASED SCIENCE TOWARDS THERAPIES THAT CAN BENEFIT PATIENTS. UP HERE YOU SEE THE CHEVRON OF THE PRODUCT DEVELOPMENT GOING FROM BASIC RESEARCH TO AT THIS POINT EARLY PHASE CLINICAL TRIALS. THIS IS THE SWEET SPOT WHERE CIRM IS ACTUALLY PROVIDING THE FUNDING, AND PARTICULARLY FOR TRANSLATIONAL RESEARCH WE FEEL A PARTICULAR NEED TO FUND THE VALLEY OF DEATH, THE BRIDGE TO CURES, WHICHEVER YOU LIKE TO TERM IT, FOR THOSE TYPES OF PROJECTS THAT ARE TRYING TO GO FROM PRECLINICAL PROOF OF CONCEPT THROUGH THE IND FILING TO ENTER FIRST-IN-HUMAN UP THROUGH EARLY PHASE CLINICAL TRIAL.

WE HAVE A VARIETY OF INITIATIVES FROM FUNDAMENTAL BIOLOGY, EARLY TRANSLATION, DISEASE

TEAM, TWO STRATEGIC PARTNERSHIPS, WHICH YOU WILL HEAR ABOUT IN OCTOBER. DISEASE TEAM I HAVE BEEN UP AND RUNNING SINCE 2010. THERE ARE NOW 13 DISEASE TEAMS THAT HAVE BEEN FUNDED FROM THAT DISEASE COHORT. ONE OF OUR DISEASE TEAMS, THE SUBJECT OF ONE OF THE REVIEWS TODAY, ACTUALLY HAS SUCCESSFULLY FILED THEIR IND AS READY TO GO TO THAT NEXT STAGE, WHICH IS CLINICAL TRIALS. WE HAVE APPROXIMATELY 70 PROJECTS IN OUR TRANSLATIONAL PORTFOLIO, APPROXIMATELY, AS I SAID, 13 DISEASE TEAMS. WE HAVE EIGHT APPROVED DISEASE TEAM THERAPY DEVELOPMENT PROPOSALS THAT YOU APPROVED BACK IN JULY AT THE ICOC. AND IN ADDITION, WE HAVE ABOUT 50 EARLY TRANSLATIONAL AWARDS FROM THE VARIOUS ITERATIONS OF THESE INITIATIVES. SO ALTOGETHER WE HAVE 71 DIFFERENT PROJECTS THAT ARE WORKING ALONG THE TRANSLATIONAL PIPELINE.

THE PURPOSE OF THIS PARTICULAR INITIATIVE, RFA 10-05, IS REALLY TO ADVANCE PRECLINICAL AND/OR CLINICAL DEVELOPMENT OF STEM CELL-BASED THERAPIES. AND THE GOAL REALLY WITHIN THE NEXT FOUR-YEAR TIME FRAME IS FOR THESE APPLICANTS TO BE ABLE TO SUBMIT A WELL-SUPPORTED IND FOR A CLINICAL STUDY AND/OR COMPLETE A PHASE I OR PHASE I-II STUDY, OR TO COMPLETE A PHASE II STUDY.

SO THE GOAL IS REALLY TO ACHIEVE ALL THIS WITHIN THE NEXT FOUR YEARS. THE SCOPE MUST BE CELL-BASED IN A SINGLE THERAPEUTIC CANDIDATE. THE CANDIDATE CAN ARISE FROM PLURIPOTENT STEM CELLS, FROM PROGENITOR CELLS, FROM REPROGRAMMED OR GENETICALLY MODIFIED STEM CELLS, ALSO FROM SMALL MOLECULES OR BIOLOGIC CANDIDATES THAT HAVE BEEN CHARACTERIZED OR GENERATED USING STEM CELLS. WE ALSO ALLOWED CANDIDATES THAT TARGET THE CANCER STEM CELL OR ENDOGENOUS STEM CELLS IN VIVO, AND ALSO ENGINEERED FUNCTIONAL TISSUE CANDIDATES FOR TRANSPLANTATION.

THERE WAS A VARIETY OF REVIEW CRITERIA THAT OUR GRANTS REVIEW GROUP CONSIDERED IN LOOKING THROUGH ALL THESE APPLICATIONS AND PROPOSALS. THEY INCLUDED THE SIGNIFICANCE AND IMPACT, THE PROJECT RATIONALE, THE THERAPEUTIC DEVELOPMENT READINESS, THE FEASIBILITY OF THE PROJECT PLAN, THE PRINCIPAL INVESTIGATOR AND THE DEVELOPMENT TEAM, WHAT KINDS OF COLLABORATIONS, RESOURCES, AND THE WORK ENVIRONMENT THEY HAD IN PLACE. AND IN ADDITION, SOME OF THESE AWARDS HAD CONDITIONS THAT WERE PLACED AT THE TIME OF THE PLANNING AWARD, AND THESE CONDITIONS WERE REVIEWED TO SEE WHETHER THEY WERE MET AT THE TIME OF THE REVIEW OF THE RESEARCH AWARD.

I WANT TO REVIEW SOME OF THE GRANT REVIEW EXPERTISE THAT WE HAVE ON BOARD. IT'S A VERY ROBUST GROUP OF EXPERTS WITH EXPERTISE ACROSS THE SPECTRUM OF PRECLINICAL STUDIES, INCLUDING PRECLINICAL TOXICOLOGY AND SAFETY, MANUFACTURING, INCLUDING CHEMISTRY AND CONTROLS, DISEASE AND CLINICAL EXPERTISE, EXPERTISE IN REGULATORY ISSUES IN TRYING TO GET A PRODUCT TO FIRST IN HUMAN AND THROUGH CLINICAL TRIALS, AND ALSO EXPERTISE IN PRODUCT DEVELOPMENT. HOW DO YOU DEVELOP A PRODUCT? WE WANTED TO MAKE SURE THAT REALLY AT THE END OF THE DAY WE'RE TRYING TO FUND RESEARCH PROGRAMS THAT HAVE THE ABILITY TO ACTUALLY BECOME A THERAPEUTIC PRODUCT.

THAT'S WHAT MAKES THIS PARTICULAR INITIATIVE DIFFERENT FROM A LOT OF OUR OTHER INITIATIVES THAT MIGHT BE MORE RESEARCH FOCUSED. THIS IS ACTUALLY FOR THOSE PEOPLE WHO CAN HIT THE GROUND RUNNING, WHO HAVE A VERY WELL-CHARACTERIZED DEVELOPMENT CANDIDATE, AND ARE REALLY ABLE TO DO THOSE STUDIES TO GO THROUGH THE IND-ENABLING STEPS TO EITHER FILE THAT IND OR TO CONDUCT THOSE CLINICAL TRIALS.

I WANT TO JUST RECAP THE RECOMMENDATIONS AND DECISIONS FROM THE JULY 26TH ICOC. I'M TRYING

TO GET RID OF THAT LITTLE THING AT THE TOP, BUT IT LIKES TO STAY THERE.

ANYWAY, THE RECOMMENDATIONS FROM THE JULY ICOC IS BASICALLY SIX PROPOSALS WERE RECOMMENDED FOR FUNDING WITH A BUDGET UP TO 113 MILLION. FIFTEEN PROPOSALS WERE NOT RECOMMENDED FOR FUNDING.

AT THE ICOC ON JULY 26TH, THE BOARD ACTUALLY ASKED CIRM MANAGEMENT OUR SCIENTIFIC ADVICE ON NINE OF THOSE APPLICATIONS, AND THEY WERE PROVIDED ADVICE THAT TWO PROPOSALS SEEMED TO DESERVE ADDITIONAL CONSIDERATION BECAUSE OF NEW DATA THAT POTENTIALLY ADDRESSED SOME KEY CONCERNS IN THE GRANT WORKING GROUP RECOMMENDATIONS. THOSE WERE THE PROJECTS THAT YOU WILL HEAR ABOUT LATER ON THE CARDIAC CLINICAL TRIAL AND ALSO ON THE DUCHENNE MUSCULAR DYSTROPHY PROPOSAL.

THE BOARD, YOU CONSIDERED THE INPUTS THAT WERE PROVIDED FROM THE GRANTS REVIEW GROUP, FROM CIRM, AND FROM PUBLIC COMMENT, AND VOTED TO APPROVE EIGHT PROPOSALS FOR FUNDING WITH A BUDGET UP TO 151 MILLION. AND THEN AS THE CHAIRMAN NOTED, ANOTHER FIVE PROPOSALS WERE SENT FOR ADDITIONAL ANALYSIS.

THESE ARE THE APPROVED AWARDS FROM JULY OF 2012. YOU SEE THE APPLICATION NUMBER ON THE LEFT, THE SCORE ON THE NEXT COLUMN, THE DISEASE AREA IN

THE MIDDLE COLUMN, THE THERAPEUTIC APPROACH IN THE NEXT COLUMN, AND THEN THE GOAL OF WHAT THEY SAID THEY WERE GOING TO DO AT THE COMPLETION OF THE FOUR YEARS.

THE TWO THAT ARE ASTERISKED AT THE BOTTOM, THE PROPOSAL WORKING ON AMYOTROPHIC LATERAL SCLEROSIS AND THE PROPOSAL WORKING ON SEVERE COMBINED IMMUNODEFICIENCY WERE MOVED TO A FUNDING LEVEL. WITH THOSE TWO ADDITIONAL PROPOSALS, THAT FUNDING THEN INCREASED FROM 113 MILLION TO 151 MILLION.

THE FIVE PROPOSALS THAT YOU REFERRED FOR ADDITIONAL ANALYSIS INCLUDED THE FOLLOWING: A PROPOSAL ON ALZHEIMER'S DISEASE USING FETAL-DERIVED NEURAL STEM CELLS WITH THE GOAL OF HAVING AN IND THAT WOULD ALLOW THE RESEARCH TO MOVE FORWARD INTO FIRST-IN-HUMAN TRIAL. YOU SEE THE ASKED FOR BUDGET ON THE RIGHT-HAND COLUMN.

THE NEXT PROPOSAL WAS IN RETINITIS PIGMENTOSA USING ALLOGENEIC RETINAL PROGENITOR CELLS. THE GOAL FOR THIS PROJECT WAS ACTUALLY TO COMPLETE A PHASE I-II CLINICAL TRIAL. THE REQUESTED BUDGET WAS TO THE TUNE OF 17.3 MILLION.

THE THIRD PROPOSAL WAS IN DUCHENNE MUSCULAR DYSTROPHY. HERE IT WAS A COMBINATION

PROJECT USING AN ANTISENSE OLIGONUCLEOTIDE AND A SMALL MOLECULE. THE GOAL HERE WAS TO CONDUCT IND-ENABLING RESEARCH TO ALLOW THEM TO FILE THAT IND TO ENTER INTO FIRST-IN-HUMAN CLINICAL TRIALS. AND THE REQUESTED BUDGET WAS 20 MILLION.

THE NEXT PROPOSAL WAS IN BREAST CANCER USING A MONOCLONAL ANTIBODY TARGETED TO A CANCER STEM CELL. THE GOAL THERE WAS TO COMPLETE PHASE I AND PHASE II CLINICAL TRIALS WITH A BUDGET REQUESTED OF 20 MILLION.

AND THEN THE LAST PROPOSAL WAS FOR A THERAPEUTIC APPROACH TO TREAT PATIENTS AFTER THEY HAD HAD A MYOCARDIAL INFARCTION. HERE THE PROPOSED GOAL WAS THE COMPLETION OF A PHASE II TRIAL. AND THEIR REQUESTED BUDGET WAS UP TO 19.8 MILLION.

JUST TO REITERATE THE ADDITIONAL ANALYSIS PROCESS, THE PURPOSE OF THAT ANALYSIS WAS REALLY TO EVALUATE SPECIFIC NEW INFORMATION THAT BECAME AVAILABLE AFTER THE GRANT REVIEW GROUP REVIEW AND DETERMINE WHETHER THAT INFORMATION ADDRESSED SOME OF THE REVIEWERS' KEY OR PRIMARY CONCERNS AND WOULD HAVE IMPACTED THE OVERALL GRANT REVIEW GROUP RECOMMENDATION FOR FUNDING THE AWARD.

FOR EACH APPLICATION THE INFORMATION PROVIDED OR REFERENCED AT THE BOARD MEETING AND

ASSOCIATED SPECIFIC ADDITIONAL MATERIAL WERE REQUESTED FROM THE APPLICANT. THIS NEW INFORMATION WAS EVALUATED IN ALL CASES BY THE GRANT REVIEW GROUP REVIEW CHAIR AS WELL AS ONE OF THE ORIGINALLY ASSIGNED REVIEWERS AND A PATIENT ADVOCATE. EACH APPLICATION WAS ASSESSED INDEPENDENTLY, AND A TELECONFERENCE WAS SCHEDULED TO DISCUSS EACH ONE. THE GOAL OF THOSE DISCUSSIONS WAS REALLY TO PROVIDE THE RESULTS AT THIS SEPTEMBER BOARD MEETING.

IN YOUR PREREAD YOU HAVE A LIST OF THE TYPES OF INFORMATION THAT WAS ASKED FOR FROM EACH OF THE APPLICANTS. I WON'T GO OVER THAT LIST OF REQUESTED INFORMATION FOR EACH OF THESE PROPOSALS, BUT YOU HAVE IT IN YOUR PREREAD.

THE RECOMMENDATIONS, THEN, I'D LIKE TO GO THROUGH AT THIS TIME. I WILL ALSO WANT TO ADD, IN ADDITION TO NEW MATERIAL, ALL OF THE REVIEWERS HAD THE ORIGINAL APPLICATION, THE REVIEW CRITIQUE, AS WELL AS THE PETITION.

SO THESE ARE THE ADDITIONAL ANALYSIS RESULTS: FOR THE ALZHEIMER'S DISEASE PROPOSAL, THE ADDITIONAL ANALYSIS RESULTS WERE THAT THEY DID NOT FEEL THE NEW INFORMATION WOULD RESULT IN A CHANGE IN THE GRANT REVIEW GROUP RECOMMENDATION, WHICH WAS NOT RECOMMENDED FOR FUNDING.

FOR THE RETINITIS PIGMENTOSA PROPOSAL WHERE THE APPROACH WAS UTILIZING ALLOGENEIC RETINAL PROGENITOR CELLS, THEY THOUGHT THAT THE NEW INFORMATION WOULD RESULT IN A CHANGE IN THE GRANT REVIEW GROUP, AND THEY DID RECOMMEND FUNDING FOR THAT PROPOSAL.

FOR THE THIRD PROPOSAL IN DUCHENNE MUSCULAR DYSTROPHY, THE APPROACH OF A COMBINED ANTISENSE OLIGONUCLEOTIDE AND A SMALL MOLECULE, THE ANALYSIS DID REVEAL THAT THEY THOUGHT IT WOULD MODIFY THE GRANT REVIEW GROUP RECOMMENDATION. AND THE RECOMMENDATION HERE WAS FOR A CONVERSION OF THIS RESEARCH PROPOSAL TO AN EARLY TRANSLATION PROJECT.

THE FOURTH PROPOSAL IN BREAST CANCER UTILIZING A MONOCLONAL ANTIBODY, THE RESULTS FROM THIS DISCUSSION OF THE NEW MATERIAL SHOWED THAT THERE WAS NO CHANGE IN THE GRANT REVIEW GROUP RECOMMENDATION, WHICH REMAINED AT A NOT RECOMMENDED FOR FUNDING.

AND THEN THE FIFTH PROPOSAL IN POST MYOCARDIAL INFARCTION HEART FAILURE FOR THE ALLOGENEIC CARDIAC-DERIVED STEM CELLS, THE DISCUSSION REVEALED A CHANGE IN THE GRANT REVIEW GROUP RECOMMENDATION TO RECOMMENDATION WITH CONDITIONS.

I'D BE HAPPY TO GO THROUGH ANY OF THE DETAILS OF WHAT THE SPECIFIC INFORMATION WAS AND WHAT THE RATIONALE WAS FOR MAKING THE RECOMMENDATION WHICH I'M BRINGING FORWARD TO YOU TODAY. THANK YOU VERY MUCH.

CHAIRMAN THOMAS: THANK YOU, DR. FEIGAL. SO --

MS. SAMUELSON: LET'S CONSIDER REVIEWING EACH OF THOSE AREAS. THAT'S MUCH BETTER. THESE ARE BIG, IMPORTANT GRANTS IN OUR PORTFOLIO. I'M NOT SURE HOW MUCH TIME IT WOULD TAKE, AND I KNOW TIME IS PRECIOUS, BUT I'D BE INTERESTED IN A BIT MORE OF AN ANALYSIS ON EACH OF THOSE.

DR. FEIGAL: SO I DID PROVIDE THE PREREAD WHICH HAD THE MATERIALS AND THE RECOMMENDATIONS. WE CAN GO THROUGH IT VERBALLY IF YOU'D LIKE.

MS. SAMUELSON: I DEFER TO YOUR WISDOM, UNDERSTANDING WHAT OUR OTHER COMPETING DEMANDS ARE, MR. CHAIRMAN, BUT...

CHAIRMAN THOMAS: BY THE WAY, I'D LIKE TO NOTE FOR THE RECORD THAT SHERRY LANSING HAS JOINED THE MEETING ON THE PHONE. WELCOME, SHERRY.

MS. LANSING: I'M HERE. I JUST WANTED YOU TO KNOW THAT. THANK YOU.

CHAIRMAN THOMAS: THANK YOU.

I THINK WITH RESPECT TO THE THREE THAT ARE RECOMMENDED FOR FUNDING, I THINK EVERYBODY HAS GOT THE PREREADS ON THOSE. I'M NOT SURE EXACTLY HOW MUCH ADDITIONAL INFORMATION THE BOARD NEEDS. HAPPY TO HAVE DR. FEIGAL GO INTO IT IN MORE DETAIL.

MS. SAMUELSON: THE ONE QUESTION ON THAT THAT ARISES IS ON THE ONE IT'S RECOMMENDING IT GO FROM A DISEASE TEAM TO EARLY TRANSLATION, WHICH IS A DRAMATIC REDUCTION IN THE SCOPE AND MONEY.

CHAIRMAN THOMAS: YES. WE'LL DO THAT. WE'LL TAKE EACH IN ORDER.

MR. SHEEHY: THAT WAS GOING TO BE MY RECOMMENDATION, THAT WE HAVE THE DISCUSSION ON EACH GRANT AS WE BRING IT UP.

CHAIRMAN THOMAS: SO WHY DON'T WE PROCEED, FIRST OFF, TO THE TWO THAT WERE RECOMMENDED FOR FUNDING. LET'S START WITH THE RP.

DR. FEIGAL: CAN WE START WITH THE ONE THAT'S ON THE --

CHAIRMAN THOMAS: YES. I THOUGHT THE EASIEST ONE WAS THE -- OKAY. LET'S GO AHEAD. LET'S START WITH THE CAPRICOR PROPOSAL. DO YOU WANT TO COMMENT FURTHER, OR SHALL WE PROCEED?

DR. FEIGAL: WHY DON'T I JUST BRIEFLY, FOR THOSE OF YOU WHO MAY NOT HAVE READ THE PREREAD, I

CAN BRIEFLY REVIEW IT BECAUSE THEY'RE ACTUALLY FAIRLY SHORT.

CHAIRMAN THOMAS: YES. THANK YOU.

DR. FEIGAL: SO THE RECOMMENDATIONS HERE THAT WERE -- LET ME START WITH THE BOTTOM LINE. THEY WERE RECOMMENDED FOR FUNDING WITH TWO CONDITIONS. ONE, TO ENSURE THE PHASE I COMPONENT OF THE PHASE I-II CLINICAL TRIAL HAS DEMONSTRATED ADEQUATE SAFETY BEFORE PROCEEDING WITH THE PHASE II, WHICH IS WHAT CIRM NORMALLY WOULD DO EVEN IF THEY HADN'T PLACED THAT CONDITION ON IT. AND, TWO, THAT THE INVESTIGATORS SHOULD FOCUS THE PHASE II COMPONENT ON PATIENTS WITH RECENT MI.

I CAN GO THROUGH, THEN, THE KEY POINTS FROM THE SUMMARY I PROVIDED, THAT THE REVIEWERS WERE CONVINCED BY THE ACHIEVEMENT OF THE KEY MILESTONES SINCE SUBMISSION THAT THE APPLICANT HAD ADDRESSED KEY CONCERNS ABOUT READINESS TO PROCEED TO A PHASE II CLINICAL TRIAL. THAT IS TO SAY THE APPLICANT HAD FILED AND HAD AN APPROVED IND BY THE FDA, THAT THEY HAD AN NIH GRANT THAT HAD BEEN AWARDED TO CONDUCT THE PHASE I COMPONENT OF THEIR PHASE I-II CLINICAL TRIAL, THAT THE APPLICANT HAD ALREADY HIRED CONSULTANTS AND A CONTRACT RESEARCH ORGANIZATION, AND HAD ALREADY LIMITED THEIR TRIAL TO THE UNITED

STATES RATHER THAN PROCEEDING TO A GLOBAL CLINICAL TRIAL, AND THAT THEY HAD ALREADY ENGAGED THE APPROPRIATE CLINICAL LEADERSHIP AND HAD DEFINED ROLES AND RESPONSIBILITIES.

SO THEY BASICALLY HAD MET KEY MILESTONES. AT THE TIME OF THE REVIEW, THE APPLICANT WAS ACTUALLY -- IT APPEARED THAT THEY WERE STILL FINISHING UP THEIR PRECLINICAL WORK ON GOOD LABORATORY PRACTICE STUDIES THAT NEEDED TO BE DONE. SO THAT ACTUALLY THERE ARE QUITE A FEW NEW MILESTONES THAT HAD BEEN MET THAT THE REVIEWERS WERE NOT AWARE OF. AND SO ONCE THOSE KEY MILESTONES THAT WERE MET WERE MADE AWARE OF BY -- THE REVIEWERS WERE MADE AWARE OF, THEY THEN DECIDED THAT THEY WERE READY TO PROCEED TO PHASE II CLINICAL TRIAL, THAT IT WASN'T A FANTASY, THAT THEY ACTUALLY DID -- THERE WASN'T ALL THAT REGULATORY UNCERTAINTY, AND THERE WASN'T THE DIFFUSENESS OF THE CLINICAL TRIAL WITH THE GLOBAL CLINICAL TRIAL THAT REVIEWERS WERE VERY CONCERNED ABOUT.

THE CONDITIONS THAT WERE PLACED THAT YOU MAY WANT TO DISCUSS IS THAT THEY WANTED THE APPLICANTS TO REALLY FOCUS THE PHASE II COMPONENT ON THE PATIENT POPULATION THAT THEY THOUGHT WOULD BE MOST READILY ABLE TO BENEFIT FROM THEIR PROPOSED

THERAPEUTIC APPROACH SO THAT THEY COULD REALLY GET TO CLINICAL PROOF OF CONCEPT WHICH WAS FELT WOULD BE VERY, VERY IMPORTANT FOR THIS TEAM TO ACHIEVE BEFORE THEY TRIED TO DO A BROADER TYPE OF CLINICAL TRIAL IN OTHER DISEASE INDICATIONS. THAT IS TO SAY, THE CHRONIC CHF WHERE THEY THOUGHT IT WAS MUCH LESS LIKELY TO SUCCEED. IT'S NOT THAT IT CAN'T SUCCEED. IT'S JUST THAT THEY THOUGHT THEIR BEST BET WAS IN RECENT MI, AND THAT SHOULD BE WHERE CIRM PLACED OUR INVESTMENT BET.

MS. SAMUELSON: AND THAT WAS THEIR CONCLUSION IN TERMS OF THE TARGET GROUP.

DR. FEIGAL: CORRECT.

MS. SAMUELSON: THEY BELIEVED THAT WAS THE APPROPRIATE TARGET GROUP?

DR. FEIGAL: THE REVIEWERS DID. THEY ALREADY HAD THE RECENT POPULATION IN THEIR PROPOSED CLINICAL TRIAL. THEY HAD TWO COHORTS, ONE WITH MORE RECENT MI AND THEN ONE WITH MORE CHRONIC MI AND CONGESTIVE HEART FAILURE WHERE THE MI HAD OCCURRED IN THE MORE DISTANT THAN IN THE RECENT MI PATIENTS.

THERE IT WAS FELT THAT, BECAUSE OF THE BIOLOGY OF HOW THE HEART REMODELS, THAT THEY WOULD HAVE THE BEST BET IN PATIENTS WITH RECENT MI THAN IN THOSE WHO HAD ALREADY HAD SCAR FORMATION.

MS. SAMUELSON: DOES THAT ENTAIL A REDUCTION IN THE SCOPE OF THE GRANT?

DR. FEIGAL: WELL, THERE ARE TWO ISSUES WITH THAT. THE BUDGET, THE WAY WE'RE PROPOSING IT IS TO REMAIN UP TO 20 MILLION BECAUSE WE GOT TWO COMMENTS FROM THE REVIEWERS. ONE, THEY THOUGHT THEY HAD UNDERESTIMATED THE AMOUNT THEY NEEDED TO BUDGET FOR A RANDOMIZED PHASE II CLINICAL TRIAL. AND, TWO, IF YOU DO HAVE A MORE FOCUSED CLINICAL TRIAL WHERE ONE OF THE COHORTS ARE NOT IN THERE, THEN YOU MIGHT REDUCE THE BUDGET. SO I CAN'T GIVE YOU AN EXACT BUDGET BECAUSE ACTUALLY THAT'S SOMETHING THAT CIRM SCIENTIFIC STAFF WOULD NORMALLY WORK WITH THE APPLICANT DURING THE PREFUNDING PHASE OF A GRANT APPLICATION TO WORK OUT THE DETAILS OF THE BUDGET.

MS. SAMUELSON: DOES STAFF HAVE A BEST ESTIMATE AT THIS POINT OF WHAT THAT WOULD ENTAIL, WHETHER A REDUCTION OR AN INCREASE?

DR. FEIGAL: WE THINK IT WOULD PROBABLY -- WE SUSPECT IT WOULD BE -- 20 MILLION WOULD BE THE CEILING, AND WE SUSPECT IT WOULD BE SOMETHING LESS THAN 20 MILLION. UNTIL WE TALK TO THE APPLICANT, WE DON'T KNOW.

MR. TORRES: SO IN OTHER WORDS, OUR CONDITIONS ARE MORE RESTRICTIVE THAN THE NIH AND THE

FDA HAVE PUT ON THIS APPLICANT?

DR. FEIGAL: THE FDA, YOU HAVE TO REMEMBER, IS LOOKING AT SAFETY, AND THE NIH ISN'T FUNDING THE PHASE II COMPONENT.

MR. TORRES: SO WHY WOULD WE PROVIDE A GRANT AND NOT LET THEM GO BEYOND A SPECIFIC POPULATION AND GET MORE BANG FOR OUR BUCK BY LETTING THEM GO BEYOND THE RESTRICTIONS THAT THE REVIEWERS THINK THEY SHOULD PROVIDE?

DR. FEIGAL: WELL, I THINK THERE WERE TWO ISSUES. ONE, THIS IS WHERE CIRM IS INVESTING THE DOLLARS, AND THEY THOUGHT THE BEST INVESTMENT FOR CIRM WAS FOR THIS GROUP TO FOCUS ON PATIENTS WITH RECENT MI. THAT WOULD BE THE COHORT OF THE PATIENT POPULATION BECAUSE THE HEART IS STILL REMODELING WHERE THIS TYPE OF THERAPEUTIC APPROACH, GIVEN HOW THE INVESTIGATORS THINK IT COULD WORK, WOULD BE THE MOST LIKELY TO BENEFIT. IT'S NOT RULING OUT THE ALSO -- BECAUSE THE MORE DISTANT CONGESTIVE HEART FAILURE PATIENTS WERE A SEPARATE COHORT OF PATIENTS WITH A SEPARATE CONTROL GROUP.

DR. PRICE: SOMEWHERE IN MY E-MAIL, AND I CAN'T FIND IT NOW TODAY, THERE WAS A SLIDE DECK WHICH WAS PROVIDED BY THE GRANTEE IN THIS CASE.

MS. LANSING: TALK A LITTLE LOUDER.

DR. PRICE: THAT SLIDE DECK APPARENTLY MADE THE CASE THAT IT WOULD BE MORE INEFFICIENT TO DO THESE THINGS SERIATIM BOTH BECAUSE OF HAVING TO REAPPLY FOR FEDERAL CLEARANCE AND FOR OTHER REASONS. AND SINCE THE GRANTEE'S REPRESENTATIVES ARE HERE IN THE AUDIENCE, MAYBE, FOR THE BENEFIT OF THE BOARD, THEY SHOULD EXPLAIN WHY THEY THINK IT WOULD BE MORE INEFFICIENT TO DO THESE AS CLINICAL TRIALS SERIATIM RATHER THAN AT THE SAME TIME.

MS. LANSING: I HAVE THE SAME QUESTION. THIS IS SHERRY. THAT'S ONE OF THE REASONS I WANTED TO BE ON BECAUSE THEY MADE THAT POINT. SO I'M CURIOUS AS TO WHY WE'RE NOT RECOMMENDING THAT.

CHAIRMAN THOMAS: OKAY. DR. FEIGAL, LET'S GO TO MR. JUELSGAARD. THEN I THINK THAT -- DR. PRIETO AFTER MR. JUELSGAARD.

DR. JUELSGAARD: SO THIS QUESTION SORT OF FALLS IN LINE WITH WHAT SENATOR TORRES WAS ASKING AND ALSO WHAT DR. PRICE WAS ASKING. SO WHAT WE'VE DONE IS IN THIS RE-REVIEW, WE'VE TAKEN A MUCH SMALLER GROUP OF INDIVIDUALS; THAT IS, THE CHAIRMAN OF THE GRANTS WORKING GROUP AND THEN ONE ADDITIONAL MEMBER WHO HAS EXPERTISE IN THIS AREA, AS IT SAYS ON THE SLIDE, PLUS A PATIENT ADVOCATE. AND SO IT BEGS THE QUESTION OF IF THERE'S A BROAD ENOUGH EXPERTISE

IN THAT SMALL GROUP TO MAKE THESE KIND OF RECOMMENDATIONS, INCLUDING LIMITING THE SCOPE OF THE PATIENTS THAT ARE GOING TO POTENTIALLY BE SUBJECTED TO A CLINICAL TRIAL.

SO THESE ARE REALLY JUDGMENT CALLS NOW AT THIS POINT, WHICH LACK THE BENEFIT THAT THE ORIGINAL LARGE GROUP GAVE WHEN IT REVIEWED THESE PROJECTS AT A PREVIOUS TIME.

DR. FEIGAL: IF I MAY SAY, JUST TO BE CLEAR, THESE COMMENTS CAME UP DURING THE ORIGINAL REVIEW. SO THESE AREN'T DE NOVO RECOMMENDATIONS THAT ARE BEING MADE. SO THIS ISN'T SOMETHING THAT HADN'T BEEN DISCUSSED. THERE WERE OTHER SEVERE ISSUES ABOUT THE APPLICATION AT THE TIME THAT ROSE TO THE TOP. THEY HADN'T FINISHED THE PRECLINICAL, THEY HADN'T EVEN FILED THE IND.

SO I HEAR WHAT YOU'RE SAYING, BUT THESE ARE NOT DE NOVO ISSUES THAT AROSE JUST WITH A SUBSET OF THE GWG.

DR. PRIETO: I GUESS MY CONCERN OR QUESTION IS WHETHER THIS DECISION TO ONLY TAKE THE RECENT MI WAS DONE WITH SOME CLINICAL EXPERTISE ON THE PART OF THE REVIEWERS. FROM MY UNDERSTANDING OF THIS GRANT AND WHAT I RECALL FROM THE ORIGINAL REVIEW, WHAT THEY'RE LOOKING AT IS THE PHENOMENON OF

REMODELING, NOT THE ACUTE VASCULAR AND THROMBOEMBOLIC EVENTS THAT HAPPEN IN MI, AND THAT'S AN ONGOING PROCESS THAT PROCEEDS FOR SOME TIME AFTER THE ACUTE EVENT. SO I'M NOT SURE THAT THAT RATIONALE OF CUTTING IT OFF AT SIX MONTHS REALLY MAKES SENSE IN THIS.

DR. FEIGAL: FIRST OF ALL, WELL, I MEAN THERE ARE TWO POINTS. ONE, THIS IS SOMETHING THAT HAD ARISEN WITH THE FULLER GROUP IN THE ORIGINAL DISCUSSION. BUT I THINK ONE OF THE THINGS THAT WE -- WE CAN DISCUSS IT FURTHER HERE. THE OTHER THING THAT WE COULD DO IS DISCUSS IT WITH THE APPLICANT IN TERMS OF WORKING IT OUT IN THE PREFUNDING DISCUSSIONS THAT WE NORMALLY DO WITH THE APPLICANT, PARTICULARLY SINCE WE'RE NOT AT THIS POINT SAYING HALVE THE BUDGET BECAUSE AT THIS TIME WE GOT RECOMMENDATIONS IN TWO DIFFERENT DIRECTIONS. ONE, WE THINK THEY UNDERBUDGETED AND, TWO, IF WE WANT A MORE FOCUSED CLINICAL TRIAL.

SO MAYBE WHAT WOULD MAKE SENSE, IT'S JUST A SUGGESTION, IS MAYBE THAT WE ACTUALLY WORK WITH THE APPLICANT ON SOME OF THESE ISSUES BEFORE THE MONEY GOES OUT THE DOOR.

CHAIRMAN THOMAS: THANK YOU, DR. FEIGAL. I THINK THAT SINCE WE'RE GETTING A LOT OF DISCUSSION

ON THIS TOPIC, THAT IT WOULD BEHOOVE US TO GET SOME COMMENT.

MR. SHEEHY: I THINK YOU WERE ABOUT TO BRING THE APPLICANT UP. I DO THINK THAT THE FRAME IN WHICH WE'RE LOOKING AT THIS PARTICULAR ISSUE IS ONE THAT THE BOARD OUGHT TO ADDRESS DIRECTLY. SO I THINK WE SHOULD WEIGH IN ON THIS ISSUE MYSELF. AND THE FRAME WAS REALLY ONE OF ECONOMIC EFFICIENCY, WHICH IS NOT ACTUALLY THE MISSION OF THIS BOARD. IF WE CAN GET TO MORE PATIENTS FASTER AND IT MAKES THE BEST SENSE CLINICALLY, THAT SHOULD BE OUR MOTIVATION.

AND I THINK IF YOU LISTEN TO DR. FEIGAL'S COMMENTS, SHE WAS TALKING ABOUT BEST INVESTMENT. AND THIS BOARD AND THIS AGENCY DOESN'T EXIST AS A VC FIRM, BUT AS ACTUALLY TO GET BENEFITS TO PATIENTS. AND MY STRONG SUSPICION IS THAT WE COULD SERVE MORE PATIENTS BETTER -- WE ARE MAKING A BET, BUT THIS WHOLE AGENCY IS A BET. WE WOULD SERVE MORE PATIENTS BETTER BY DOING THE LARGER GROUP IS KIND OF THE SENSE THAT I'M GETTING. BUT REALLY THE FRAME WITH WHICH THIS PARTICULAR RECOMMENDATION WAS MADE WAS ECONOMIC EFFICIENCY, NOT BEST OUTCOMES FOR PATIENTS.

SO I JUST WANT TO PUT THAT PARTICULAR -- I THINK IF WE COULD HEAR FROM THE APPLICANTS, THAT

WOULD BE GREAT.

CHAIRMAN THOMAS: DR. TROUNSON.

DR. TROUNSON: WELL, I'M NOT SURE I AGREE WITH JEFF ON THAT. I THINK, AS ELLEN HAS SAID, THE PATIENTS THAT HAVE HAD THE EARLY MI ARE MORE LIKELY TO RESPOND. AND SO I THINK IT WAS TAKEN AT THAT BASIS, THAT ESSENTIALLY IF YOU WERE ABLE TO SHOW THAT YOU GET A RESPONSE WITH THOSE PATIENTS, THEN IT WOULD GIVE YOU HEART TO GO AND TREAT THE PATIENTS THAT HAD THE MORE CHRONIC CONDITIONS. SO THAT'S THE WAY THAT THE REVIEWERS EXPLAINED IT.

THE SENSE THAT WE UNDERBUDGETED WAS SOMETHING THAT WAS A CONCERN TO THEM, BUT BASICALLY IF YOU'RE ABLE TO GET THE INFORMATION ON THE MORE LIKELY RESPONDER, THAT WOULD GIVE YOU MORE HEART TO WANT TO CONTINUE TO TREAT THE MORE CHRONIC CONDITION. SO THAT WAS -- WE'RE ASKED TO GIVE YOU THAT INFORMATION, AND THAT'S THE WAY I VERY CLEARLY HEARD THE INFORMATION DIRECT.

MR. SHESTACK: DR. FEIGAL, I FEEL LIKE YOU ARE PRESENTING A THIRD POSSIBILITY IN A WAY, A WAY OF SORT OF WORKING THROUGH A PROCESS WHEN YOU TALK ABOUT THE PREFUNDING PROCESS, WHICH SEEMS INTERESTING TO ME AND IN LINE WITH WHAT I THINK PART OF OUR MISSION IS, WHICH IS LOOKING TO HELP OUR

APPLICANTS SUCCEED. SO COULD YOU JUST EXPLAIN TO ME AND ANYONE ELSE WHO DOESN'T KNOW HOW THAT PROCESS WORKS, AND WHAT ARE SOME OF THE MOVEMENTS THAT CAN HAPPEN DURING THAT PREFUNDING PROCESS?

DR. FEIGAL: IN THE PREFUNDING REVIEW, WHICH IS NOT -- I'M NOT CREATING IT DE NOVO. THIS IS SOMETHING WE ALWAYS DO. WE WORK WITH THE APPLICANT TO GO THROUGH MUTUALLY AGREED MILESTONES, WE GO THROUGH THEIR BUDGETS, WE LOOK AT ACTIVITIES, ASCERTAIN WHAT'S APPROPRIATE, WHAT'S REALLY NEEDED IN TERMS OF WHAT THEY NEED TO GET DONE TO REACH THEIR MILESTONES, HELP THEM WITH THINKING THROUGH THE SUCCESS CRITERIA, THEIR PROGRESS MILESTONES, CRITERIA FOR THAT. SO WE GO THROUGH ALL OF THE DIFFERENT CONDITIONS, AND THEN ALL OF THAT INFORMATION IS PART OF THE NOTICE OF GRANT AWARD WHEN IT GOES OUT. SO THAT BEFORE ANY MONEY GOES OUT THE DOOR, WE HAVE THESE ITERATIVE DISCUSSIONS WITH THE APPLICANT.

MR. SHESTACK: SO, IN EFFECT, IT IS SOMEWHAT OF A REFINEMENT OF THE PROPOSAL AT THE VERY END?

DR. FEIGAL: WELL, IT'S IN ORDER TO IMPLEMENT IT. SO WE HAVE TO HAVE MORE DETAIL IN TERMS -- AND MAKE SURE WE'RE IN MUTUAL AGREEMENT

ABOUT WHAT WE'RE DEFINING AS IMPORTANT MILESTONES, THE CRITERIA, AND THE ACTIVITIES THAT THEY NEED TO GET THERE, AND THE BUDGET THAT GOES WITH IT.

MR. SHESTACK: THANK YOU.

CHAIRMAN THOMAS: I WOULD LIKE, SINCE THE ISSUE THAT HAS SORT OF BEEN PUT ON THE TABLE HERE IS THE VIABILITY OF THE PROCEDURE WITH RESPECT TO CHRONIC PROBLEMS, I THINK THIS IS A GOOD TIME TO GET TO PUBLIC COMMENT, HEAR FROM DRS. LITVAK AND DR. MARBAN AND MARBAN ON THIS SUBJECT BECAUSE THAT WOULD INFORM THIS DISCUSSION. PLEASE REMEMBER IN YOUR PUBLIC COMMENT, YOU ARE CONFINED TO THREE MINUTES. DR. LITVAK, WELCOME.

DR. LITVAK: THANK YOU VERY MUCH. I'LL LIMIT MY COMMENTS TO THREE MINUTES.

FIRST OF ALL, I WANT TO GO ON THE RECORD AND THANK THE CIRM CLINICAL AND SCIENTIFIC LEADERSHIP FOR THEIR PATIENCE AND DILIGENCE IN HELPING US -- HELPING THE PROCESS ON ALL THESE RE-REVIEWS. THEIR EFFORTS SHOULD BE DULY NOTED.

I WANT TO MAKE A COUPLE OF POINTS HERE BEFORE I INTRODUCE THE GENTLEMAN BEHIND ME. WE'RE VERY GRATEFUL AND WE'RE EXCITED ABOUT DOING THIS IMPORTANT STUDY. I PERSONALLY RECOMMENDED, WHEN I JOINED THE COMPANY, ADDING THE LATER GROUP. I DON'T

WANT TO CALL THEM A CHRONIC GROUP, THE LATER GROUP. THE ORIGINAL GROUP IS ZERO TO SIX MONTHS OR ONE MONTH TO SIX MONTHS AND THE LATER GROUP IS SIX MONTHS TO A YEAR.

THE ORIGINAL DISTINCTION WAS, IN FACT, SOMEWHAT ARTIFICIAL. THERE REALLY IS NO MECHANISTIC DISTINCTION BETWEEN SOMEBODY WHO'S FOUR MONTHS OUT AND SOMEBODY WHO'S EIGHT MONTHS OUT.

LET'S LOOK AT THE MECHANISM OF ACTION AS WE UNDERSTAND IT. WE KNOW FROM THE CADUCEUS TRIAL THAT THE MECHANISM OF ACTION OF OUR THERAPY IS THAT IT REDUCES SCAR SIZE AND PROMOTES REGENERATION OF HEART MUSCLE CELLS. OUR GOAL IS TO INTERFERE WITH THE PROCESS THAT ALAN DISCUSSED, WHICH IS REMODELING, WHICH IS THE ENLARGEMENT OF THE HEART THAT OCCURS AFTER LARGE HEART ATTACKS. THAT PROCESS DOESN'T TAKE DAYS OR WEEKS. IT TAKES YEARS TO OCCUR.

WHAT WE'RE TRYING TO DO IS INTERFERE EARLY ON. THE REASON I WANTED TO GO AND ADD THIS MORE -- OLDER COHORT WAS IT VASTLY EXPANDS THE NUMBER OF PATIENTS THAT WE CAN INCLUDE IN THE CLINICAL TRIAL AND THE NUMBER OF PATIENTS THAT WE ULTIMATELY CAN ADDRESS. THE INFRASTRUCTURE OF DOING THIS WITH ONE TRIAL ALLOWS US TO BE EXTREMELY EFFICIENT IN TERMS

OF COST. IT'S ONE TRIAL, IT'S ONE APPROVAL, IT'S ONE ADMINISTRATION, ONE SET OF DATABASES, ETC., ETC. IT ALSO SAVES YEARS. IF WE WANT TO GO TO A PHASE III IN THREE YEARS, WE NEED TO HAVE THE BEST PATIENT POPULATION IDENTIFIED. IF WE SPENT THREE YEARS DOING AN ARTIFICIAL GROUP FIRST AND THEN THREE MORE YEARS DOING THE OTHER GROUP LATER, WE'RE SIX YEARS AWAY FROM A PHASE III, AND WE'RE DELAYING THERAPY TO PATIENTS.

WE'RE VERY, VERY FOCUSED ON DELIVERING THERAPY TO PATIENTS. I WASN'T -- OBVIOUSLY WE'RE NOT PRIVY TO THE RATIONALE OF THE INDIVIDUALS ON THE REVIEW COMMITTEE. WE'RE GRATEFUL TO THEM. I'M SPEAKING FROM THREE POINTS OF VIEW. NO. 1, AS A CARDIOLOGIST, I'VE TREATED A LOT OF PATIENTS POST INFARCTION. THEY START TO DETERIORATE IN THE END OF THE FIRST YEAR AND IN THE SECOND YEAR. WE NEED TO INTERRUPT THAT PROCESS.

NO. 2, AS A BUSINESSPERSON, TALK ABOUT INVESTMENT. I'VE BEEN SUCCESSFUL IN BUSINESS. THIS IS THE BEST BUSINESS APPROACH FOR US BECAUSE IT APPROACHES THE LARGEST ADDRESSABLE MARKET THAT WE POSSIBLY CAN IN THE FASTEST WAY.

FINALLY, AS ALL OF YOU KNOW, I AM A PASSIONATE BELIEVER IN THE MISSION OF CIRM, AND THAT

MISSION IS TO GET THERAPIES TO AS MANY PATIENTS AS POSSIBLE AS FAST AS POSSIBLE. SO THAT'S WHY I PROPOSE THAT.

I'D LIKE TO INTRODUCE DR. TIM HENRY. DR. HENRY CAME ALL THE WAY FROM MINNESOTA TO SPEAK TO YOU TODAY. HE'S THE PRINCIPAL INVESTIGATOR OF THIS ALL STAR TRIAL. HE IS CERTAINLY THIS COUNTRY'S MOST EMINENT CLINICAL RESEARCHER IN CARDIAC STEM CELLS AND PROBABLY IN THE WORLD. AND HE'S GOING TO GIVE HIS POINT OF VIEW.

DR. HENRY: THANK YOU, MR. CHAIRMAN. REALLY APPRECIATE THE OPPORTUNITY TO SAY A FEW WORDS. FIRST OF ALL, I'LL START BY WE HAVE HAD -- I'M THE DIRECTOR OF RESEARCH AT MINNEAPOLIS HEART INSTITUTE AND A PROFESSOR AT THE UNIVERSITY OF MINNESOTA. WE ARE ALSO ONE OF THE PRINCIPAL INVESTIGATORS FOR THE NIH-SPONSORED STEM CELL CENTER. SO WE HAVE EXTENSIVE EXPERIENCE WITH HUMAN CARDIOVASCULAR STEM CELLS, OVER TEN CELLS, OVER 30 CLINICAL TRIALS, AND OVER 400 PATIENTS THAT WE'VE ACTUALLY TREATED IN MINNEAPOLIS. SO HAVE A LOT OF EXPERIENCE WITH TRIAL DESIGN.

AND I THINK FROM MY PERSPECTIVE, THIS IS CLEARLY RIGHT NOW THE SINGLE MOST EXCITING TRIAL FOR TREATMENT FOR CARDIOVASCULAR STEM CELLS FOR ACUTE

MYOCARDIAL INFARCTION. I THINK I REALLY WANT TO EMPHASIZE THREE KEY POINTS. NO. 1, IT'S BASED ON REALLY EXCELLENT PRECLINICAL DATA AND REALLY EXCELLENT PHASE I DATA.

AND THEN THE THIRD THING, I THINK THE TRIAL DESIGN IS VERY UNIQUE, BUT I REALLY WOULD LIKE TO EMPHASIZE THIS HAS REALLY GONE UNDER EXTENSIVE REVIEW WITH BOTH THE NIH AND THE FDA AND IS APPROVED THIS WAY. AND I THINK THE -- IT ALLOWS TO PUT IN THE PHASE I SAFETY TRIAL, WHICH IS ACTUALLY SPONSORED BY THE NIH, TOGETHER WITH THE PHASE II TRIAL, WHICH WILL TAKE A LOOK AT -- I ALSO WOULD NOT REALLY CALL IT CHRONIC. IT'S REALLY DIVIDING ACUTE MYOCARDIAL INFARCTION WITHIN THE FIRST YEAR AND ALLOWS US TO REALLY LOOK AT THE TWO TIME PERIODS WITHIN THE FIRST YEAR, BUT BOTH WOULD REALLY BE RECENT. WE'RE REALLY NOT LOOKING AT CHRONIC HEART FAILURE PATIENTS IN THIS SITUATION.

SO FROM MY PERSPECTIVE, IT'S A VERY EXCITING DESIGN THAT'S ALREADY APPROVED BY THOSE OTHER AGENCIES, AND WE'RE REALLY READY TO START WITHIN THE NEXT FEW MONTHS. AND IT WOULD MAKE IT VERY EFFICIENT TO DO IT AS THE TRIAL IS CURRENTLY DESIGNED. THANK YOU.

CHAIRMAN THOMAS: THANK YOU, DR. HENRY.

ADDITIONAL PUBLIC COMMENT?

MR. SOGUES: LADIES AND GENTLEMEN, GOOD AFTERNOON. MY NAME IS EDWARD SOGUES (PHONETIC), AND I'M SUPPOSED TO BE A DEAD MAN. AND I'M HERE ALIVE TODAY IN FRONT OF YOU. IN AUGUST 2012 I HAD A MASSIVE HEART SURGERY, AND I WAS RUSHED TO CEDARS-SINAI HOSPITAL. IN THE EMERGENCY ROOM, WHILE AN EKG WAS BEING PERFORMED ON ME, THE DOCTOR WAS VERY BRUTAL WHILE READING THE EKG. HE SAID, "YOUR HEART IS DYING. WE HAVE TO GET YOU IMMEDIATELY INTO SURGERY." THAT WAS THE BEGINNING OF MY RECOVERY BECAUSE FOUR STINTS WERE INSTALLED IN MY HEART IN THE FOLLOWING TWO WEEKS. AND THEN I HAD ONE OF THE ARTERY CLOGGED 80 PERCENT, THE OTHER ONE CLOGGED 100 PERCENT, AND THE INSTALLATION OF THE STINTS WAS OBVIOUSLY EXTREMELY IMPORTANT.

WHILE I WAS AT THE HOSPITAL RECOVERING, A DOCTOR ENTERED IN MY ROOM AND SAID HE WAS PART OF CADUCEUS, WHICH WAS A STEM CELL RESEARCH PROGRAM. HE EXPLAINED TO ME THE BENEFITS THAT THEY WERE TRYING TO ACHIEVE THROUGH THIS RESEARCH AND ASKED ME IF I WOULD BE PART OF THAT RESEARCH. I FOUND THE IDEA MIND BOGGLING BECAUSE I THOUGHT THAT THIS WAS REALLY GOING TO THE FOREFRONT OF SCIENCE, AND I THOUGHT THAT IT WAS AN AMAZING, AMAZING AVENUE. AND

I THOUGHT THAT I WOULD HAVE LIKED IN MY OWN MODEST WAY TO BE PART OF IT.

WHEN I LEFT THE HOSPITAL, I DID AS MUCH RESEARCH AS I COULD, READING AND GOING THROUGH MEDICAL EXPERT OPINIONS, AND I DECIDED ULTIMATELY TO VOLUNTEER. I WENT THROUGH THE REMOVAL OF MY HEART'S CELLS THROUGH BIOPSY. MY CELLS WERE GROWN IN LABORATORY TO A SIZABLE NUMBER, AND THEN THEY WERE REINSERTED INTO MY HEART IN A SOLUTION. AND THIS WAS IN THE CYCLE OF ONE AND A HALF MONTH. AND THEN I CONTINUED THROUGH ALL THE TRIAL TESTS IN THE FOLLOWING MONTHS.

AND IN THE SAME TIME, I HAD MY OWN CARDIOLOGIST FOLLOWING ME. AND I USED TO VISIT MY CARDIOLOGIST ON A REGULAR BASIS MONTHLY, AND 11 MONTHS ALMOST AFTER MY HEART ATTACK I WAS VISITING MY DOCTOR, AND A TECHNICIAN CAME INTO THE ROOM AND PERFORMED AGAIN EKG, WHAT HE USED TO DO IN THE BEGINNING OF EVERY SESSION. AND LIKE A CLOCKWORK, I ASKED HIM, BECAUSE I WAS ALWAYS COURTEOUS, "HOW DOES IT LOOK LIKE?" AND HE LOOKED AT MY CHART, HE LOOKED INTO MY FILE, AND SAID, "YOU ARE SUPPOSED TO HAVE HAD A HEART ATTACK, RIGHT? BUT NOTHING HERE INDICATES YOU HAD ONE." THAT WAS THE GREATEST MOMENT OF TRIUMPH I COULD EVER GO THROUGH.

I RECENTLY BECAME GRANDFATHER LAST WEEK. I'D LIKE THIS TO BE AVAILABLE TO EVERYONE. THANK YOU VERY MUCH.

CHAIRMAN THOMAS: THANK YOU.

(APPLAUSE.)

CHAIRMAN THOMAS: DR. MARBAN.

DR. MARBAN: EDUARDO MARBAN. I WOULD LIKE TO OFFER SOME COMMENTS BASED ON MY POSITION AS HAVING BEEN THE PRINCIPAL INVESTIGATOR OF THE DISEASE TEAM THAT LED TO THE IND THAT PROVIDED THE BASIS FOR THIS TRIAL. ONE HAS TO DO WITH THE SCIENCE, AND THE OTHER HAS TO DO WITH CIRM'S GRANT OPERATING POLICIES.

WITH REGARD TO THE SCIENCE, WE HAVE HAD SOME VERY INTERESTING GLIMMERS THAT, EVEN THOUGH CADUCEUS FOCUSED ON RELATIVELY RECENT MI'S IN THE THREE-MONTH-OLD TIME FRAME, SOME OF OUR PATIENTS, SIX OF OUR PATIENTS ACTUALLY HAD PREVIOUS HEART ATTACKS THAT WERE OLD. UNFORTUNATELY THEY HAD A NEW HEART ATTACK ON TOP OF AN OLD ONE. AND IF YOU POSITED THAT THE STUFF ONLY WORKED ON THE RECENT ONE, WE HAD AN INTERNAL CONTROL BUILT INTO THOSE PATIENTS ANATOMICALLY. WE COULD COMPARE THE RESPONSES IN THE NEW INJURY AND THE OLD INJURY, AND PRECISELY THE SAME RESPONSES WERE SEEN IN THE OLD

INJURY AS IN THE NEW INJURY, RESORPTION OF ABOUT HALF OF THE SCAR AND REGROWTH OF NEW HEART MUSCLE.

SO THAT SELF-VALIDATES TO ME THE PREMISE THAT PERHAPS WE SHOULD BROADEN THE ELIGIBILITY CRITERIA.

THE OTHER STORY WAS IN A PATIENT WHO WAS THE VERY FIRST PATIENT RANDOMIZED TO RECEIVE THE CARDIOSPHERE-DERIVED CELLS. HE UNFORTUNATELY SUFFERED FROM A MANUFACTURING FAILURE, BUT HE STAYED IN THE TRIAL. IN THE PROCESS OF DOING SO HAD FOUR BASELINE MAGNETIC RESONANCE IMAGES THAT SHOWED THAT HE HAD 33 PERCENT OF HIS HEART TURN TO SCAR. HE THEN CAME TO ME AND SAID, "DR. MARBAN, I'D LIKE YOU TO ASK THE FDA FOR EXTRAORDINARY PERMISSION FOR ME TO UNDERGO A SECOND BIOPSY AND ACTUALLY GET MY HEART CELLS IN AN OPEN LABEL THING 14 MONTHS AFTER MY HEART ATTACK." I SAID, "I'LL BE HAPPY TO ASK THE FDA BECAUSE YOU'VE BEEN SUCH A LOYAL SUBJECT, BUT IT'S UNLIKELY THAT THEY'LL SAY YES."

THEY SAID YES. HE HAD A BIOPSY, HE GOT TREATED, AND HIS SCAR SIZE WENT FROM 33 PERCENT TO 19 PERCENT.

SO THESE ARE VERY CONVINCING SCIENTIFIC FACTS THAT TO ME TELL ME WE SHOULD BROADEN THE CRITERIA.

THE COMMENT ABOUT CIRM HAS TO DO WITH THE FACT THAT AS THE PI OF A DISEASE TEAM, I'VE HAD REGULAR INTERACTIONS WITH CIRM STAFF. AND THE INTERACTIONS WITH CIRM STAFF ARE RIGOROUS, AND I WOULD SAY THAT THEY'RE THOROUGH AND PROACTIVE. AND THAT TO PUT ADDITIONAL CONDITIONS, PRECONDITIONS, ON THIS GRANT WOULD BE A MISTAKE. I THINK I WOULD BEG THE ICOC TO JUST APPROVE IT BECAUSE IT IS A WONDERFUL, WONDERFUL STUDY, AND WE WILL DO THE CITIZENS OF CALIFORNIA A GREAT SERVICE, AND WE WILL MAKE A VICTORY FOR CIRM IF WE DO THIS. THANK YOU.

CHAIRMAN THOMAS: ANY OTHER PUBLIC COMMENT? OKAY. DO I HEAR A MOTION?

DR. PRICE: I HAVE A MOTION TO APPROVE THIS DISEASE TEAM PROPOSAL AND LIFT THE CONDITIONS THAT WERE ESTABLISHED BY THE REVIEW COMMITTEE.

MR. JUELSGAARD: I SECOND THAT MOTION.

CHAIRMAN THOMAS: I THINK, IF I CAN JUST CLARIFY, THE FIRST CONDITION I DON'T BELIEVE YOU ARE REFERRING TO BECAUSE THAT WAS SORT OF A BENIGN WE ALWAYS DO THAT CONDITION.

DR. FEIGAL: EVEN IF YOU TELL US TO LIFT IT, WE WON'T. WE HAVE TO MAKE SURE THE PHASE I SAFETY IS ENSURED.

CHAIRMAN THOMAS: SO YOU'RE REFERRING TO

THE SECOND CONDITION, WHICH IS THE LENGTH OF TIME FROM THE MI IN THE COHORTS TO BE EVALUATED. OKAY. FURTHER DISCUSSION BY MEMBERS OF THE BOARD ON THE MOTION?

MS. LANSING: I HOPE I HEARD ENOUGH OF THIS. SO WE'RE ALL COMFORTABLE, THEN, THAT WE SHOULDN'T DO IT ALL AT ONCE AS DR. LITVAK TALKED ABOUT?

CHAIRMAN THOMAS: NO. THE MOTION WAS THAT WE DO DO IT ALL AT ONCE.

MS. LANSING: OKAY. THAT'S WHAT I WAS HOPING YOU WOULD SAY, BUT I COULDN'T HEAR IT RIGHT. SO THE MOTION IS THAT WE DO IT ALL AT ONCE AS DR. LITVAK SUGGESTED IN HIS COMMENTS?

MR. TORRES: IN THAT CASE VOTE AYE.

CHAIRMAN THOMAS: THAT'S CORRECT.

MS. LANSING: THANK YOU. I'M HAVING TROUBLE HEARING. I APOLOGIZE. I'LL SECOND THAT.

CHAIRMAN THOMAS: OKAY.

DR. LUBIN: SO COULD YOU PLEASE SAY WHY -- GIVE THE COMMENT THAT THE REVIEWERS FELT SO STRONGLY ABOUT THAT WE'RE DISMISSING BY THE COMMENTS WE'VE JUST HEARD?

DR. FEIGAL: JUST SO YOU'RE CLEAR, IN THE DESIGN THAT THE APPLICANTS ARE PROPOSING -- EVEN IN

THE DESIGN THAT THE APPLICANTS ARE PROPOSING, IT'S TWO COHORTS. THERE'S THE EARLY COHORT AND THERE'S THE LATER COHORT. SO THEY'RE GOING TO BE ANALYZING THEM WITH DIFFERENT CONTROL ARMS RELEVANT TO THAT COHORT. SO THEY ARE TREATING THEM SEPARATELY. THE EFFICIENCY IS THAT THEY'LL GO TO THE SAME SITES, AND THE SINGLE IRB COULD BE UTILIZED FOR GOING THROUGH IT.

THE RATIONALE, PRESUMABLY WHY THE RATIONALE WHY IT'S TWO COHORTS RATHER THAN ONE IS THAT THEY TOO THINK THAT THERE MIGHT BE -- I DON'T MEAN TO READ INTO THEM; BUT SINCE THEY DID DO IT AS TWO COHORTS, THAT THERE ARE SOME DIFFERENCES IN HOW THE REMODELING TAKES PLACE. AND SO THEY DO WANT THE ABILITY TO ANALYZE THEM SEPARATELY.

MS. SAMUELSON: MR. CHAIRMAN, ISN'T THERE ALSO A MATTER OF PATIENT NEED AND URGENCY COMPELLING THE EXPANSION OF THE TRIAL BECAUSE MORE MIGHT WELL BE LEARNED RATHER THAN WAITING?

DR. FEIGAL: ALL I CAN SAY IS THAT PEOPLE WHO LOOKED AT IT AND LOOKED AT THE EVIDENCE THAT WAS PROVIDED THOUGHT THE MOST LIKELY PLACE WHERE THIS PROJECT COULD ACHIEVE BENEFIT WAS IN THE MORE RECENT MI COHORT, THAT IT COULD BE A SMALLER, MORE QUICKLY RUN TRIAL, AND THEY COULD GET TO THEIR ANSWER

SOONER. BUT I THINK IF THE ARGUMENT IS ECONOMIC EFFICIENCY, THAT'S A DIFFERENT SET OF QUESTIONS. AND I THINK WE ALSO UNDERSTAND CHRONIC HEART FAILURE, AND I KNOW THAT DR. LITVAK ISN'T CONSIDERING SIX MONTHS TO 12 MONTHS THE ENTIRE POPULATION OBVIOUSLY OF CONGESTIVE HEART FAILURE.

I THINK IN A MARKETING ISSUE, IT'S OBVIOUSLY FOR INVESTORS VERY, VERY INTERESTED IN THE POPULATION THAT'S MUCH BIGGER, THOSE WHO HAVE HAD A CHRONIC CONDITION WELL AFTER A HEART ATTACK. IT'S JUST THAT THE REVIEWERS FELT THAT THEIR BEST BET FOR ACTUALLY HAVING A POSITIVE BENEFIT FOR THE PATIENTS WHO ENROLL IN A TRIAL WOULD BE IN THAT MORE RECENT COHORT.

OFTEN WHEN WE DESIGN CLINICAL TRIALS, YOU TRY TO DESIGN IT SO THAT THE HOPE IS YOU'RE DESIGNING IT FOR THE PATIENT WHO MIGHT POTENTIALLY BENEFIT.

CHAIRMAN THOMAS: CALLING THE QUESTION. MARIA, PLEASE READ THE ROLL ON THIS.

MR. HARRISON: CHAIR, COULD I JUST RESTATE THE MOTION SO IT'S CLEAR FOR THE RECORD? THE MOTION IS TO APPROVE FUNDING FOR APPLICATION 5735 WITHOUT THE SECOND CONDITION REGARDING THE NATURE OF THE COHORT.

CHAIRMAN THOMAS: THANK YOU, MR. HARRISON. MARIA, PLEASE ROLL CALL VOTE.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: YES.

MS. BONNEVILLE: DAVID BRENNER. JACOB LEVIN.

DR. LEVIN: YES.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: MARCY FEIT.

MS. FEIT: YES.

MS. BONNEVILLE: MICHAEL FRIEDMAN. LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG. SAM HAWGOOD.

DR. HAWGOOD: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: SHERRY LANSING.

MS. LANSING: YES.

MS. BONNEVILLE: BERT LUBIN.

DR. LUBIN: YES.

MS. BONNEVILLE: MICHAEL MARLETTA. PHIL PIZZO. CLAIRE POMEROY.

DR. POMEROY: YES.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: CARMEN PULIAFITO.

DR. PULIAFITO: YES.

MS. BONNEVILLE: ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.

MS. SAMUELSON: YES.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: YES.

MS. BONNEVILLE: JONATHAN SHESTACK.

MR. SHESTACK: YES.

MS. BONNEVILLE: OSWALD STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: YES.

MS. BONNEVILLE: JAMES ECONOMOU.

DR. BRENNER.

DR. BRENNER: I THOUGHT I SAW A LETTER FROM SOMEONE FROM UCSD THAT WOULD BE A CONFLICT FOR ME.

MR. HARRISON: IT'S NOT, BUT YOU'RE FREE TO ABSTAIN.

DR. BRENNER: I'M HAPPY TO VOTE YES.

CHAIRMAN THOMAS: THE MOTION PASSES. CONGRATULATIONS.

(APPLAUSE.)

DR. FEIGAL: THAT WAS ONE.

CHAIRMAN THOMAS: WHY DON'T WE -- WHICH DO YOU HAVE NEXT UP HERE, THE DUCHENNE? YOU WANT TO PROCEED TO THAT, ELLEN?

DR. FEIGAL: ACTUALLY WHAT I'D LIKE TO DO IS HAVE IT -- FOR SOME REASON IT'S FROZEN.

MS. LANSING: JAMES, AM I RECUSED FROM THE OTHER ONES?

CHAIRMAN THOMAS: JAMES, SHERRY WAS ASKING IF SHE'S CONFLICTED.

DR. FEIGAL: WHILE SHE'S TRYING TO PULL THAT ONE UP --

MS. LANSING: I THINK I AM.

DR. POMEROY: OTHER UC'S ARE, SO YOU ARE BY DEFINITION, SHERRY.

DR. FEIGAL: SO THE NEXT ONE IS THE PROPOSAL ON THE RETINITIS PIGMENTOSA. AND THIS ONE, BASICALLY IT WAS RECOMMENDED FOR FUNDING. AND THEY JUST SUGGESTED THAT THERE BE A CIRM MANAGEMENT SITE

VISIT. THE KEY CONCERNS FROM THE GRANT REVIEW GROUP HAD PRIMARILY BEEN THAT THE APPLICANT WAS SUGGESTING A TWO-PRONGED APPROACH FOR DEVELOPMENT OF A THERAPY, STARTING FIRST WITH A GOOD TISSUE PRACTICE LEVEL OF MANUFACTURING AND THEN CHANGING TO GOOD MANUFACTURING PROCESS.

THEY WERE ASKED TO PROVIDE A CERTAIN AMOUNT OF NEW INFORMATION ABOUT WHERE THEY REALLY WERE WITH THE MANUFACTURING PROCESS OF THIS THERAPEUTIC PRODUCT. THE REVIEWERS TOOK A LOOK AT IT. THEY WERE CONVINCED BY THE DATA THEY RECEIVED THAT THE MANUFACTURING WAS AT A GOOD MANUFACTURING PRACTICE LEVEL OF DEVELOPMENT. THEY DID, HOWEVER, SUGGEST THAT CIRM DO A SITE VISIT TO GAIN MORE IN-DEPTH KNOWLEDGE ABOUT THE MANUFACTURING AND THE RESEARCH PROJECT STATUS.

MR. TORRES: SO MOVED AS RECOMMENDED.

CHAIRMAN THOMAS: IS THERE A SECOND?

MS. GIBBONS: SECOND.

CHAIRMAN THOMAS: SECONDED BY LEEZA. MOVED BY SENATOR TORRES. DO WE HAVE DISCUSSION ON THIS BY MEMBERS OF THE BOARD? JOAN.

MS. SAMUELSON: WHAT WOULD THE SITE VISIT -- WHAT WOULD THE INCLUSION OF THE SITE VISIT THEN ENTAIL? MIGHT THAT --

DR. FEIGAL: THAT'S NOT A CONDITION. THEY JUST RECOMMENDED THAT -- WE CAN DO A SITE VISIT WITHOUT ANYBODY SUGGESTING IT TO US. WHAT IT WOULD BE, WHAT WE'D LIKE TO DO IS GO OVER SOME MORE OF THE DETAILS ABOUT THE MANUFACTURING, USUALLY THEIR STANDARD OPERATING PROCEDURES. THERE'S A PARTICULAR AMOUNT OF ASSAYS AND CRITERIA THAT NEED TO BE IN PLACE IN ORDER TO HAVE GOOD MANUFACTURING. SO IT'S BASICALLY JUST GOING OVER SOME OF THESE MORE IN-DEPTH DETAILS, INFORMATION THAT WASN'T REQUESTED AT THE TIME OF THE ADDITIONAL ANALYSIS, BUT THINGS AS A FUNDING AGENCY WE WANT TO WORK OVER WITH THE APPLICANT TO MAKE SURE ALL THESE DETAILS WERE ACTUALLY IN PLACE.

MS. SAMUELSON: SURE. BUT IT'S NOT ASSUMED THAT THAT WOULD SIGNIFICANTLY CHANGE THE SCOPE OR COST OF THE GRANT?

DR. FEIGAL: I THINK THIS WOULD BE SOMETHING WE WOULD NORMALLY WANT TO DO WITH THE APPLICANT IS GO OVER SOME OF THESE ISSUES PARTICULARLY SINCE THE APPROACH WAS SORT OF UNUSUAL IN THE WAY IT GOT PRESENTED IN THE APPLICATION. SO WE JUST WANT TO MAKE SURE THAT THINGS WERE GOING IN THE RIGHT DIRECTION. SO, NO, WE DON'T SEE IT AS A SHOWSTOPPER AT ALL.

CHAIRMAN THOMAS: THIS IS NOT MEANT TO BE LIMITING. IT'S A PROCESS THING HERE AND IS NOT A PRECONDITION AT ALL.

FURTHER DISCUSSION BY MEMBERS OF THE BOARD? HEARING NONE, DO WE HAVE PUBLIC COMMENT ON THIS ITEM? HEARING NONE, MARIA, PLEASE DO A ROLL CALL FOR THIS ITEM.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: YES.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: YES.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. BONNEVILLE: SAM HAWGOOD.

DR. HAWGOOD: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: BERT LUBIN.

DR. LUBIN: YES.

MS. BONNEVILLE: CARMEN PULIAFITO.

DR. PULIAFITO: YES.

MS. BONNEVILLE: ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.

MS. SAMUELSON: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: JONATHAN SHESTACK.
MR. SHESTACK: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: KRISTINA VUORI.
DR. VUORI: YES.
CHAIRMAN THOMAS: THANK YOU. THE MOTION CARRIES. CONGRATULATIONS.
DR. FEIGAL: THIRD PROPOSAL IS FOR THE COMBINATION THERAPY, AN ANTISENSE OLIGONUCLEOTIDE AND A SMALL MOLECULE. THIS ADDITIONAL ANALYSIS RESULTED IN A MODIFIED GRANT REVIEW GROUP RECOMMENDATION. AS YOU RECALL, IT WAS NOT RECOMMENDED FOR FUNDING AS A DISEASE TEAM. THE ADDITIONAL ANALYSIS, AGAIN, AGREED IT SHOULD NOT BE RECOMMENDED FOR FUNDING AS A DISEASE TEAM. HOWEVER, THEY RECOMMENDED THE APPLICANTS BE ALLOWED TO REVISE THE PROPOSAL ALONG THE LINES OF AN EARLY TRANSLATIONAL AWARD WITH A REDUCED SCOPE AND BUDGET WITH TOTAL BUDGET APPROXIMATELY UP TO WHAT WE

NORMALLY HAVE FOR AN EARLY TRANSLATION AWARD, DIRECT COSTS USUALLY APPROXIMATELY $3.5 MILLION IN DIRECT COST. WE GUESSTIMATED IT WOULD BE AROUND A CEILING TOTAL OF SIX MILLION. BUT OBVIOUSLY WE NEED TO CHECK IT WITH THE INSTITUTIONAL ISSUES IN TERMS OF INDIRECTS. AND THAT CIRM FUND THE REVISED PROPOSAL.

ONE OF THE KEY CONCERNS THAT AROSE FROM THE GRANT REVIEW GROUP REVIEW OF THE ORIGINAL APPLICATION HAD FOCUSED ON THE LACK OF ANY DEMONSTRABLE CLINICAL BENEFIT AT 24 WEEKS FROM THE RANDOMIZED CLINICAL TRIAL IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY.

THIS WAS A PHASE II-B TRIAL OF THE SINGLE AGENT, ANTISENSE OLIGONUCLEOTIDE, IN PATIENTS WITH DMD. THE FACT THAT THIS TEAM, THE APPLICANT, WANTED TO DO A COMBINATION THERAPY WITH THIS PARTICULAR ANTISENSE OLIGONUCLEOTIDE PLUS A SMALL MOLECULE AND THE AGENT IN THAT COMBINATION, THE ANTISENSE, NOT DEMONSTRATING CLINICAL BENEFIT WAS THOUGHT TO BE A VERY SIGNIFICANT ISSUE AND DIMINISHED THE RATIONALE FOR THE COMBINATION APPROACH.

ANOTHER KEY CONCERN HAD BEEN ON THE INTERACTIONS OF THE APPLICANT WITH THE COMPANY AS CIRM WAS BEING ASKED TO PAY FOR ALL OF THE MANUFACTURING COST OF THE ANTISENSE OLIGONUCLEOTIDE.

AT A 12-WEEK UPDATE FROM A PRESS RELEASE, WHICH WAS COMPANY SPONSORED, THE REVIEWERS RECEIVED INFORMATION THAT WAS CONTAINED IN THAT COMPANY-SPONSORED PRESS RELEASE AT THE 36-WEEK MARK OF THE PHASE II-B TRIAL. THIS IS DATA THAT WASN'T AVAILABLE AT THE TIME OF THE INITIAL REVIEW. AND AT THAT 12-WEEK UPDATE -- AND, BY THE WAY, THERE WILL BE ANOTHER 12-WEEK UPDATE IN OCTOBER. AT THAT 36-WEEK UPDATE, IT SHOWED A STATISTICALLY SIGNIFICANT BENEFIT AS MEASURED BY THE SIX-MINUTE WALK TEST OF THE HIGHER DOSE OF SINGLE AGENT ANTISENSE OLIGONUCLEOTIDE.

SO THE REVIEWERS, THE ADDITIONAL ANALYSIS REVIEWERS, HAD THIS INFORMATION IN HAND WHEN THEY LOOKED AT THE DATA THIS TIME. AND ALTHOUGH THEY FELT THAT IT WAS PROMISING, THEY EXPRESSED CONCERN ABOUT THE CONTROLS AND THE METHODS OF ANALYSIS. THIS IS A VERY SMALL TRIAL. IT'S 12 PATIENTS TOTAL, BUT IT'S ALSO AN ORPHAN DISEASE, BUT IT'S A VERY SMALL NUMBER OF PATIENTS, A TOTAL OF FOUR ON THAT HIGHER DOSE. TWO PATIENTS WHO RAPIDLY PROGRESSED IN THEIR DISEASE ON THE LOWER DOSE ARM OF THIS ANTISENSE OLIGONUCLEOTIDE WERE NOT INCLUDED IN THE ANALYSIS.

SO AT ANY RATE, THE REVIEWERS THOUGHT IT'S

INTERESTING, BUT IT'S PRELIMINARY. IT'S NOT COMPELLING. IT'S CERTAINLY WORTHY OF FURTHER INVESTIGATION.

THE COMPANY IS PROCEEDING WITH THE SINGLE AGENT ANTISENSE OLIGONUCLEOTIDE FOR THE DMD INDICATION. THE APPLICANT WANTS TO DEVELOP A COMBINATION PRODUCT, BUT THE REVIEWERS DID NOT FEEL THEY HAD RECEIVED ANY COMPELLING PRELIMINARY DATA ON DYSTROPHIN AND WHETHER THE SMALL MOLECULE THAT'S GOING TO BE USED IN THE COMBINATION WITH THE ANTISENSE OLIGONUCLEOTIDE COULD ACTUALLY INCREASE THE DYSTROPHIN LEVELS.

THE APPLICANT NOTED THAT THE SMALL MOLECULE COULD POTENTIALLY REQUIRE LESS ANTISENSE OLIGONUCLEOTIDE TO GET TO THE SAME LEVEL OF DYSTROPHIN. AND ALTHOUGH THIS WAS FELT TO BE A POTENTIALLY INTERESTING ECONOMIC RATIONALE, THEY WERE NOT CONVINCED THAT THIS WOULD HAVE ANY CLINICAL IMPACT.

ANOTHER CONCERN FROM THE GRANT REVIEW GROUP REVIEW HAD BEEN ON THE IMPACT TO THE HEART. THESE REVIEWERS DISCUSSED THIS ISSUE. THEY FELT THE SMALL MOLECULE IS SKELETAL MUSCLE SPECIFIC, BUT IT WAS NOT FELT TO BE A RATE LIMITING POINT. AND THE REVIEWERS AGREED THAT ANY BENEFIT TO RESPIRATORY

FUNCTION COULD HAVE A GOOD IMPACT AND THAT THE CARDIAC CONCERN WOULD BE A SECOND ORDER ISSUE.

OVERALL, THE REVIEWERS THOUGHT THE PROPOSAL WAS NOT READY FOR A DISEASE TEAM AWARD, BUT THEY DID FEEL STRONGLY THAT CIRM SHOULD INVEST IN A REVISED PROPOSAL THAT WAS FOCUSED ON FURTHER UNDERSTANDING THE COMBINATION APPROACH AS A POTENTIAL THERAPEUTIC CANDIDATE.

THE INTENT OF FUNDING A REVISED PROPOSAL AT THE LEVEL OF AN EARLY TRANSLATION AWARD WOULD BE TO ENSURE THAT THE SCIENTIFIC QUESTIONS FOR THE COMBINATION CANDIDATE ARE ADEQUATELY ADDRESSED AND THAT THE APPLICANTS ARE ABLE TO GET ANY BUSINESS RELATIONSHIPS APPROPRIATELY ALIGNED.

CHAIRMAN THOMAS: THANK YOU, DR. FEIGAL. WILL YOU JUST DESCRIBE THE PROCESS YOU WOULD UNDERTAKE TO REFINE THIS AS AN EARLY TRANSLATION AWARD?

DR. FEIGAL: SO THIS WOULD NOT GO BACK TO A REVIEW. WHAT THIS WOULD ENTAIL IS WE WOULD SEND THEM THE PARAMETERS AND THE BUDGET GUIDELINES FOR WHAT WE CURRENTLY CALL OUR EARLY TRANSLATIONAL AWARD. WE ACTUALLY HAVE PRECEDENCE FOR DOING THIS IN THE PAST. AND THAT THEY ACTUALLY SEND US A REVISED PROPOSAL WITH A SCOPE THAT'S CONSISTENT WITH

AN EARLY TRANSLATION AWARD, TRYING TO LOOK AT PRECLINICAL PROOF OF CONCEPT AND TRYING TO DEVELOP A DEVELOPMENT CANDIDATE, AND A REVISED BUDGET THAT'S APPROPRIATE TO THE SCOPE OF ACTIVITIES. AND THAT WE WOULD REVIEW IT INTERNALLY AND WORK WITH THE APPLICANT IN TERMS OF MOVING THAT FORWARD.

CHAIRMAN THOMAS: THANK YOU. DO I HEAR A MOTION ON THIS PROPOSAL?

MR. SHEEHY: I WOULD MOVE --

MR. SHESTACK: I WOULD MOVE THAT WE APPROVE UNDER THE CONDITIONS THAT HAVE BEEN SPECIFIED SO FAR.

CHAIRMAN THOMAS: MOVED BY MR. SHESTACK.

DR. LUBIN: SO I HAVE CONCERNS WITH THE STRATEGY.

CHAIRMAN THOMAS: IS THERE A SECOND TO THAT MOTION?

MR. SHEEHY: SECOND.

CHAIRMAN THOMAS: SECONDED BY DR. SHEEHY. DR. LUBIN.

DR. LUBIN: SO --

CHAIRMAN THOMAS: DID I JUST ELEVATE MR. SHEEHY TO DR. SHEEHY? CONGRATULATIONS.

DR. LUBIN: SO IT JUST IT SEEMS TO ME WE'RE REWRITING THE GRANT, THE APPLICATION, AND

WE'RE NOT LETTING IT GO THROUGH A REVIEW PROCESS THAT EVERYONE ELSE WOULD HAVE TO GO THROUGH. DOES EVERYONE FEEL COMFORTABLE WITH THAT? THAT'S WHAT WE'RE ASKING, THAT THE RECOMMENDATION WAS, WELL, THIS IS MORE EARLY TRANSLATIONAL. IF THEY SUBMITTED IT NOW, WOULD IT PASS -- SAY THEY DIDN'T DO THIS OTHER AND THEY JUST SUBMITTED IT STRAIGHT, WOULD IT PASS THE REVIEW AND THEN GET A SCORE? SO IT JUST SEEMS ODD.

NOW, MAYBE WE'VE DONE THIS BEFORE AND I'M NOT FAMILIAR WITH THAT, BUT I JUST QUESTION THE PROCESS HERE.

MR. SHEEHY: IF YOUR GOAL IS TO RUN A FAIR -- A GAME, THEN I GUESS YOU'RE RIGHT. I GUESS IF YOUR GOAL IS TO GET THE BEST OUTCOME FOR PATIENTS, THEN I THINK THIS IS AN INNOVATIVE WAY TO DO THIS. WE HAVE A CLEAR NEED HERE. WE HAVE A NEW PIECE OF INFORMATION THAT VALIDATES THEIR APPROACH, BUT THERE WAS A SENSE THAT THEY WERE NOT QUITE READY TO TAKE THIS INTO THE DISEASE TEAM CONSTRUCT, WHICH IS FAIRLY RIGID AND IS SUPPOSED TO GET US TO AN IND.

NOW, DO WE TELL THOSE KIDS WITH DMD AND THEIR PARENTS THAT OVER THE STRONG RECOMMENDATIONS OF EXPERIENCED REVIEWERS, WE THINK THEY OUGHT TO WAIT AND COME BACK A YEAR AND A HALF, TWO YEARS

LATER TO GET THIS PROJECT STARTED WHEN IT SEEMS TO HAVE A FAIRLY EASY -- THE QUESTIONS THAT THEY NEED TO ANSWER IN THIS EARLY TRANSLATION GRANT ARE FAIRLY ANSWERABLE. AND IF THEY ANSWER THEM SUCCESSFULLY, THEY WILL BE BACK HERE WITH THE DISEASE TEAM APPLICATION, AND WE WILL HAVE THE OPPORTUNITY TO MAKE A DRAMATIC DIFFERENCE IN THE LIVES OF THESE KIDS.

SO TO ME IT'S NOT A QUESTION OF WHETHER WE'RE BEING LIKE THE NIH. WE ARE NOT THE NIH, AND WE SHOULDN'T ASPIRE TO BE THE NIH. WE HAVE A SHORT CLOCK. WE ARE HERE TO MAKE A DIFFERENCE IN THE LIVES OF PATIENTS AS QUICKLY AS WE CAN. WE HAVE A VERY INTERESTING PIECE OF SCIENCE THAT HAS SHOWN, I THINK, TREMENDOUS BENEFIT, AT LEAST IN THOSE HANDFUL OF PATIENTS WHO GOT TREATED IN THAT CLINICAL TRIAL, AND I THINK IT BEHOOVES US TO BE AS AGGRESSIVE AS POSSIBLE. SO THAT WOULD BE MY VIEW ON THAT QUESTION.

DR. STEWARD: THANK YOU. I'M NOT GOING TO ARGUE AGAINST THE MOTION, BUT I AM GOING TO ARGUE AGAINST THE PROCESS IN THE FOLLOWING WAY. THIS CAME UP AT THE LAST BOARD MEETING. I DON'T THINK THAT WE SHOULD BE MAKING DECISIONS BASED ON PRESS RELEASES FROM COMPANIES. IT'S JUST NOT SOMETHING THAT WE CAN

JUDGE.

NOW, HAVING SAID THAT, THE GRANTS WORKING GROUP HAS GONE BACK AND LOOKED AT THE SCIENCE AND THE FEASIBILITY OF THE PROCESS. AND I'M COMFORTABLE WITH THE RECOMMENDATION THAT THEY MADE, ALTHOUGH, LIKE DR. LUBIN, I'M A LITTLE BIT UNCOMFORTABLE WITH THE PROCESS OF THIS GOING FORWARD, BUT I THINK WE HAVE DONE IT IN THE PAST, AND YOU CAN SPEAK TO THAT.

I DO WANT TO SAY THAT I PERSONALLY DON'T WANT TO GET INTO A SITUATION WHERE WE'RE SETTING A PRECEDENT THAT SOMEBODY CAN COME UP WITH A PRESS RELEASE JUST BEFORE OUR BOARD MEETING AND INFLUENCE THE VOTES OF THIS BOARD. IT'S NOT SCIENTIFIC EVIDENCE.

MR. SHESTACK: I THINK THAT'S SORT OF -- IF I THOUGHT THAT THAT WAS JUST WHAT HAD HAPPENED, I WOULDN'T BE SUCH A STRONG ADVOCATE FOR THIS POSITION. BUT I THINK THAT THE INFORMATION WAS AUTHENTIC INFORMATION, AND THE COMPANY PRESENTED IT, AND THE GRANTS WORKING GROUP COMMITTEE THAT DID RECONSIDERATION HAD AMPLE OPPORTUNITY TO EXAMINE IT, AND DECIDED THAT IT WAS SIGNIFICANT NEW DATA, WHICH I THINK IT WAS. AND THAT IS WHAT WE ARE HERE TO RATIFY, TO AGREE ON. WAS THERE SIGNIFICANT NEW DATA PRESENTED BETWEEN THE TIME OF THE ORIGINAL PROPOSAL

AND THE TIME OF THE GRANT WORKING GROUP DECISION? AND THE ANSWER IS -- AFTERWARDS THE ICOC MEETING, AND THE ANSWER IS THERE WAS.

DR. STEWARD: WELL, SO LET ME ASK BECAUSE I'M NOT SURE THAT THAT'S WHAT THE RECOMMENDATION OF THE GRANTS WORKING GROUP WAS BASED ON. I ACTUALLY THINK THE GRANTS WORKING GROUP RECOMMENDATION WAS BASED ON A REVIEW OF THE SCIENCE AND THE EVIDENCE THAT WAS PRESENTED AND INDEPENDENT OF THE PRESS RELEASE. AGAIN, I'M NOT ARGUING AGAINST THE MOTION. I'M JUST NOT WILLING TO VOTE ON SOMETHING POSITIVELY ON THE BASIS OF A PRESS RELEASE.

COULD YOU CLARIFY THAT, WHETHER THE GRANTS WORKING GROUP RE-REVIEW ACTUALLY CONSIDERED THAT NEW INFORMATION AS BEING A CRITICAL FACTOR IN THEIR RECOMMENDATION TO FUND IT AS AN ET, EARLY TRANSLATION?

DR. FEIGAL: WELL, I THINK IT CERTAINLY WAS AN IMPORTANT FACTOR SINCE THERE HAD BEEN NO EVIDENCE OF CLINICAL BENEFIT FROM THE PRIOR. AND JUST TO CLARIFY, I KNOW WE'RE ALL SKEPTICAL ABOUT PRESS RELEASES. THIS ACTUALLY WAS A PREDEFINED TIME OF RELEASE OF DATA. THERE'S GOING TO BE ANOTHER PREDEFINED RELEASE OF DATA IN OCTOBER FOR THIS CLINICAL TRIAL AT 48 WEEKS. SO REGARDLESS OF

WHETHER WE HAVE A BOARD MEETING, THEY'RE SUPPOSED TO COME OUT AT A 12-WEEK SEGMENT TO GIVE AN UPDATE OF THE RESULTS.

SO THESE ARE SOMETHING THE COMPANY SAID THEY WERE GOING TO DO. I KNOW SKEPTICAL PEOPLE CAN SAY IT WAS TIMED VERY BEAUTIFULLY TO BE TWO DAYS BEFORE THE BOARD MEETING, BUT THAT IS WHEN 36 WEEKS WAS UP IN TERMS OF PRESENTING THE DATA. AND IN OCTOBER THE NEXT 12-WEEK SEGMENT IS GOING TO BE UP, AND WE'LL SEE SOMETHING NEW IN OCTOBER FOR THAT.

SO YOU'RE RIGHT. WE DIDN'T SEE A REPORT, WE DIDN'T SEE A PAPER. WE JUST SAW A DESCRIPTION THAT WAS A LITTLE BIT MORE ELABORATED ABOUT THE PRESS RELEASE. BUT WE WOULD HAVE LIKED TO HAVE SEEN MORE INFORMATION, AND WE WOULD HAVE LIKED TO HAVE SEEN EVIDENCE THAT THE APPLICANT HAD ACTUALLY WORKED WITH THE COMPANY TO PERHAPS TRY AND GET MORE INFORMATION THAT COULD HAVE BEEN AVAILABLE TO US. BUT IT WAS AN ISSUE BECAUSE THAT WAS A KEY ISSUE AT THE TIME OF THE GRANTS REVIEW GROUP REVIEW. IT WAS NOT THE ONLY ISSUE. THESE OTHER ISSUES ALSO WERE IMPORTANT ABOUT THE DYSTROPHIN LEVELS AND ABOUT WHAT WAS THE LEVEL OF EVIDENCE TO SHOW THAT THIS SMALL MOLECULE -- THERE WAS AN ISSUE THAT IT COULD INCREASE EXON SKIPPING, BUT THERE WASN'T GOOD

EVIDENCE THAT IT INCREASED DYSTROPHIN LEVELS. THESE ARE SOME OF THE QUESTIONS THAT THIS EARLIER TYPE OF TRANSLATION AWARD COULD ADDRESS.

CHAIRMAN THOMAS: DR. TROUNSON, THEN MS. GIBBONS, AND THEN MR. JUELSGAARD.

DR. TROUNSON: I THINK THE BOARD NEEDS TO CONCENTRATE ON THE SMALL MOLECULE. THE COMPANY IS TAKING THE OLIGONUCLEOTIDE FORWARD. AND THERE IS NOW SOME INFORMATION THAT THAT HAS SOME POSITIVE BENEFITS. WHETHER WE CAN SORT OF SEE THAT IN THE LONGER TERM, AT LEAST SOME EVIDENCE THAT THAT PARTICULAR OLIGONUCLEOTIDE COULD BE TESTED BECAUSE THERE WAS A SECOND ONE THAT'S EVEN FURTHER FORWARD THAT WAS SHOWING SOME BENEFIT.

SO IT'S REALLY THAT IT'S THE SMALL MOLECULE. DOES THE SMALL MOLECULE BENEFIT? AND THERE WAS NO DATA PRESENTED THAT SHOWED THAT DYSTROPHIN LEVELS WOULD BE INCREMENTED WITH THAT SMALL MOLECULE. SO THAT'S WHY THE REVIEWERS SAID THEY'RE VERY SUPPORTIVE OF THIS APPROACH WITH THIS GROUP OF PATIENTS, BUT THEY HAVE TO SHOW THAT THERE'S SOME BENEFIT BY THIS SMALL MOLECULE. OTHERWISE YOU GOT NO GAME. THERE IS NO GAME HERE FOR A CLINICAL TRIAL. SO DROP BACK INTO THE TRANSLATION AND GET THE DATA, BRING IT FORWARD WITH

THE BENEFITS, AND THEN WE'VE GOT SOMETHING THAT WE CAN DEAL WITH.

I THINK IT'S THE SECOND SMALL MOLECULE THAT'S THE REALLY KEY PART. YEAH, COMBINED WITH ONE OR OTHER OF THOSE, I'D SUGGEST OLIGONUCLEOTIDES, BUT BOTH NOW SEEM TO BE WORKING. THE EXON SKIPPING MOLECULES SEEM TO BE WORKING. BUT DOES THE SMALL MOLECULE PROVIDE THE BENEFIT? AND THAT'S WHAT THE REVIEWERS WERE NOT CONVINCED ABOUT. THERE WAS NO INFORMATION THAT SAID THAT THIS WAS A BETTER APPROACH THAN EITHER ONE OF THOSE TWO THAT ARE ALREADY GOING FORWARD.

CHAIRMAN THOMAS: MS. GIBBONS.

MS. GIBBONS: JUST A COUPLE QUICK QUESTIONS, DR. FEIGAL. YOU SAID THERE WAS PRECEDENCE FOR US HAVING DONE THIS BEFORE. COULD YOU REMIND US OF WHAT THAT WAS? AND ALSO WHAT IS THE LIKELY BUDGET ADJUSTMENT GOING TO EARLY TRANSLATIONAL?

DR. FEIGAL: WELL, LET ME ANSWER YOUR FIRST QUESTION FIRST. IS THAT THE PRECEDENCE HAS BEEN AN APPLICATION THAT WAS REVIEWED AS A DEVELOPMENT CANDIDATE AT THE TIME OF ACTUALLY ONE OF THESE BOARD MEETINGS NOT TOO LONG AGO. IT WAS DECIDED THAT IT REALLY WASN'T AT A DEVELOPMENT

CANDIDATE STAGE. GO BACK TO WHAT WE CALL MORE OF A PRECLINICAL PROOF OF CONCEPT. SO IT'S NOT EXACTLY ANALOGOUS, BUT WE DO HAVE SOME PRECEDENTS OF CHANGING IT TO THE MORE APPROPRIATE LEVEL OF PRODUCT DEVELOPMENT WITH THE APPROPRIATE BUDGET THAT GOES WITH IT.

AND THEN YOUR SECOND QUESTION?

CHAIRMAN THOMAS: DR. FEIGAL, JUST ADD ON THAT THAT THE THING THAT'S COMMON HERE IS THAT THIS WAS RECOMMENDED BY THE SCIENTISTS IN THE GRANTS WORKING GROUP TO RECAST. AND THAT, I THINK, IS A KEY THING TO NOTE HERE, THAT UPON CONSIDERATION, THAT WAS FELT TO BE THE WAY TO GO.

DR. FEIGAL: YEAH. IT'S ACTUALLY MORE RIGOROUS. THE OTHER APPROACH WAS ACTUALLY DECIDED DURING THE BOARD MEETING. THIS IS ACTUALLY COMING AS A RECOMMENDATION FROM THE REVIEWERS.

MS. GIBBONS: SO IT GOES FROM THE 20 MILLION THAT WAS REQUESTED FOR DISEASE TEAM TO SIX FOR EARLY TRANSLATIONAL?

DR. FEIGAL: WHAT WE HAVE TO DO IS WORK OUT WHAT THE INSTITUTIONAL INDIRECTS ARE. IT'S $3.5 MILLION DIRECT COST, AND WE'D HAVE TO WORK OUT -- WE ARE GUESSTIMATING IT'S APPROXIMATELY SIX MILLION TOTAL, AND IT'S A THREE-YEAR AWARD, NOT A FOUR-YEAR

AWARD.

MS. SAMUELSON: I'M WONDERING IF WE HAVE ANY SORT OF ESTIMATE FOR THE TOTAL TIME THAT WOULD BE REQUIRED TO RUN IT THROUGH THE EARLY TRANSLATION PROCESS AND THEN COME BACK TO DISEASE TEAM, WHICH IS ABOUT A TWO-YEAR WORKUP TO GET TO FUNDING DECISION AS I'M REMEMBERING IT. AT THAT POINT WE'RE PAST TEN YEARS OF PROP 71, AND I'M NOT SURE IF WE HAVE ANY MONEY LEFT OR TIME. I HOPE WE DO, OF COURSE, HAVE BOTH. BUT I'M NOT SURE IF I'M ASKING FOR DATA HERE OR SEEING THAT WE'RE GOING TO HAVE TO START MAKING THOSE JUDGMENT CALLS, AND THAT WE'RE GOING TO NEED TO KNOW HOW WE RANK THE MOST IMPORTANT THINGS THAT WE'RE DOING THAT COULD HAVE A THERAPEUTIC IMPACT.

CHAIRMAN THOMAS: I THINK THAT'S GOING TO BE AN ONGOING DEBATE. I THINK WE NEED TO CONFINE OUR ANALYSIS HERE TO THE SPECIFICS.

MS. SAMUELSON: AND MY ONLY ADDITIONAL THOUGHT ON THAT IS THIS IS A SPECIFIC TREATMENT THAT MAY JUST COME TOO LATE FOR OUR MISSION.

CHAIRMAN THOMAS: WE HAVE TO PROCEED --

DR. JUELSGAARD: SO I WOULD JUST LIKE SOME CLARIFICATION ON EXACTLY WHAT THE MOTION IS. SO WHEN I LOOKED AT THE RECOMMENDATION OF THE GRANTS WORKING GROUP, SMALLER, MORE NARROWLY COMPRISED,

THEY SAID DON'T FUND AS A DISEASE TEAM APPLICATION, BUT RATHER, IN ESSENCE, KICK IT BACK TO THE PEOPLE, THE INSTITUTION, THAT ORIGINALLY SOUGHT TO HAVE THIS BE A DISEASE TEAM APPROACH AND RESTYLE IT IN A TRANSLATIONAL CONTEXT.

SO MY UNDERSTANDING IS THEIR RECOMMENDATION WAS NOT AT THIS POINT TO APPROVE IT WITH FUNDING FOR EARLY TRANSLATION, BUT RATHER PUT THE ONUS BACK ON THE PEOPLE WHO ORIGINALLY BROUGHT THIS FORWARD.

DR. FEIGAL: NO, THAT'S NOT TRUE. THEY ACTUALLY DID RECOMMEND FUNDING THE REVISED PROPOSAL.

DR. JUELSGAARD: BUT YOU DON'T KNOW WHETHER THE PEOPLE WHO PRESENTED THIS REALLY WANT TO BE FUNDED AS A REVISED PROPOSAL. HAVE YOU ASKED THEM?

DR. FEIGAL: I MEAN OUR FIRST STEP WAS TO ASK YOU BECAUSE WE DON'T WANT TO ASK SOMETHING OF THE APPLICANT BEFORE WE EVEN KNOW IF IT'S AN OPTION.

CHAIRMAN THOMAS: SO IN RESPONSE TO MR. JUELSGAARD'S VERY VALID POINT, I IMAGINE THERE ARE PEOPLE HERE WHO COULD GIVE PUBLIC COMMENT THAT COULD ANSWER THAT QUESTION. SO COULD WE TURN TO MEMBERS OF THE PUBLIC WHO WISH TO COMMENT, STARTING ON THAT POINT. PLEASE, AGAIN, CONFINE YOUR COMMENTS TO

THREE MINUTES.

DR. NELSON: THANK YOU. IT'S GOOD TO SEE YOU ALL AGAIN. I'M STANLEY NELSON. I'M A PHYSICIAN SCIENTIST AT UCLA, AND I REPRESENT AN OUTSTANDING TEAM OF SCIENTISTS AT UCLA, INCLUDING THE CO-DIRECTOR OF THIS PROJECT, CARRIE MACELI, APRIL PYLE, LEAD STEM CELL SCIENTIST, AND TOPHAN PARMAN (PHONETIC), WHO'S ONE OF OUR CRO TEAM LEADERS AT SRI.

I'D LIKE TO POINT OUT THAT THE CEO, CHRIS GARABEDIAN, AND THE EXECUTIVE DIRECTOR OF PRECLINICAL DEVELOPMENT FROM SAREPTA, THE COMPANY IN QUESTION, WERE BOTH HERE AT THE PREVIOUS ICOC MEETING, BUT GIVEN THE TENOR OF THAT, WE DIDN'T ELECT TO HAVE EVERYBODY SPEAK, BUT THEY REMAIN HIGHLY COMMITTED TO DEVELOPING EXON SKIPPING THERAPIES FOR DUCHENNE MUSCULAR DYSTROPHY AND REMAIN A COMMITTED PARTNER FOR THIS.

FIRST, WE'D LIKE TO SAY THANK YOU. IT'S A VERY RIGOROUS REVIEW PROCESS. WE APPRECIATE THE IDEA THAT IT COULD COME BACK TO THE GRANTS REVIEW GROUP IN A SMALL WORKING GROUP TO RECONSIDER NEW DATA THAT CAME UP AND SORT OF RECONSIDER THE PACKAGE. WE ARE OKAY -- I THINK THIS IS PERHAPS GETTING TO YOU, MS. SAMUELSON -- WE'RE OKAY WITH THE

LOGIC AND THE IDEA OF MOVING THIS TO AN EARLY TRANSLATIONAL THEME AWARD. MUCH OF WHAT WE WERE DOING IN THE FIRST YEAR OF THE PROPOSAL WAS DOING EXACTLY THAT.

SO IT'S A RELATIVELY MODEST MODIFICATION TO THE PROPOSAL FOR WHAT'S BEING PROPOSED. AND WE WOULD IN OUR EFFORTS IN WORKING WITH THE CIRM STAFF PUSH TO DO THAT IN AN EXPEDITED TIME FRAME BECAUSE WE DO BELIEVE IN THE URGENCY OF THIS MISSION AND WISH TO COME BACK FOR, INDEED, FUNDING THE PRE-IND ENABLING STUDIES THAT ARE EXPENSIVE AS WELL AS THE EARLY CLINICAL TRIAL WORK THAT WILL ULTIMATELY COME FROM THIS.

I HAD A FEW COMMENTS. DO YOU WANT ME TO JUST MAKE THE COMMENTS AS A CONTINUOUS? IT'S ALMOST AS IF THERE'S A DISCUSSION, SO I DIDN'T WANT TO OVERSTATE.

CHAIRMAN THOMAS: WHY DON'T YOU CONTINUE; BUT, AGAIN, YOU HAVE THREE MINUTES.

DR. NELSON: PERFECT. I WILL GO QUICKLY. ONE OF THE THINGS THAT WE WOULD LIKE TO INDICATE IS OUR PROPOSAL WAS ONE OF TWO PROPOSALS THAT FROM THE JULY MEETING INITIALLY IDENTIFIED BY THE ICOC AS HAVING SUBSTANTIAL POTENTIAL NEW DATA FOR RECONSIDERATION BY A SUBCOMMITTEE OF THE GRANTS

WORKING GROUP. WE PRESENTED FINDINGS THAT WERE SUBMITTED TO US AND ACTUALLY PUBLICLY AVAILABLE FROM SAREPTA WHICH IS DATA. IT'S NOT A PRESS RELEASE. IT'S NOT A VAGUE DESCRIPTION. IT'S ACTUALLY INDIVIDUAL PATIENT-LEVEL DATA OF SIX-MINUTE WALK TEST. THAT WAS WHAT WAS RELEASED AT THE 36-WEEK TIME POINT.

THIS WAS COUPLED WITH DATA THAT THEY RELEASED AND PUBLICLY PRESENTED ON THE INDUCTION OF DYSTROPHIN, WHICH IS FUNDAMENTALLY THE ROOT CAUSE OF THE DISEASE, WHICH WAS PRESENTED AT 24 WEEKS, WHICH ELLEN HAD JUST INDICATED AS WELL. THIS COUPLED WITH OUR OWN PRECLINICAL DATA INDICATING THE SYNERGY BETWEEN THE SMALL MOLECULE AND THEIR CLINICAL AGENT IN A MODIFIED FORM, WHICH IS SKIP EXON 23 IN THE MOUSE WHICH REPAIRS THE MOUSE DEFECT. SO WE CAN SEE DYSTROPHIN INDUCTION OF THE MOUSE DYSTROPHIN FOR EXON 23, AND WE CAN SEE THAT NOW. ACTUALLY WE HAVE SOME RECENT FUNCTIONAL DATA WHICH WAS TOO LATE TO INCLUDE IN THIS UPDATE.

MR. HARRISON: IF YOU'D TRY TO WRAP UP YOUR COMMENTS, WE'D APPRECIATE IT.

DR. NELSON: PERFECT. SO I WOULD JUST SAY WE FEEL CONFIDENT WITH MOVING THIS FORWARD. WE FEEL COMFORTABLE WITH WORKING WITH THE CIRM STAFF. WE'RE

THANKFUL OF THAT OPPORTUNITY FOR MOVING IT FORWARD. AND WE WOULD EXPECT TO BE MOVING FORWARD WITH ADDITIONAL GRANTS TO FUND THIS INTO THE LATER STAGES AS WELL.

CHAIRMAN THOMAS: THANK YOU. OTHER COMMENTS BY MEMBERS OF THE PUBLIC? OTHER COMMENTS BY MEMBERS OF THE BOARD?

DR. LUBIN: SO AS A PEDIATRICIAN AND SOMEONE WHO SEES MUSCULAR DYSTROPHY AT OUR HOSPITAL, I'M CERTAINLY NOT OPPOSED TO ANYBODY THAT'S DOING RESEARCH THAT COULD POTENTIALLY HELP CHILDREN AND PEOPLE WITH MUSCULAR DYSTROPHY. I JUST FEEL THAT IF THE PRELIMINARY DATA SUPPORTS THIS IN THE CLINICAL TRIALS THAT'S GONE THROUGH A RIGOROUS STAGE FOR EARLY TRANSLATION, I WOULD DEFINITELY SUPPORT IT. I JUST HAVE SOME CONCERNS; BUT I THINK ONCE WE EMBARK UPON A THREE-YEAR TERM, THEN WE'RE FUNDING FOR THREE YEARS.

I THINK OUR RESPONSIBILITY, BESIDES FUNDING SCIENCE THAT HELPS PEOPLE, IS TO USE THE MONEY THAT OUR TAXPAYERS HAVE GIVEN US WISELY. AND SO THAT'S WHY I RAISED THIS CONCERN.

DR. TROUNSON: CHAIR, CAN I JUST POINT OUT THAT DR. CLASSEN'S STUDY IN TRANSLATION WAS ONLY A YEAR GOING BEFORE HE CAME TO A DISEASE TEAM. HE

SPOKE TO ME ABOUT THE PACE IN WHICH HE WAS TRAVELING, AND I SUGGESTED THAT HE APPLY FOR A DISEASE TEAM. YOU JUST AWARDED THAT TO HIM AFTER ONE YEAR IN TRANSLATION.

SO THIS TEAM CAN MOVE WITH THAT KIND OF PACE. THERE'S NO REASON WHY WE WOULDN'T BE ABLE TO DO THAT APPROPRIATELY. AND I THINK THAT WAS THE SPIRIT AND THE WAY WE DISCUSSED THIS PROJECT WHEN WE RE-REVIEWED IT.

CHAIRMAN THOMAS: THANK YOU, DR. TROUNSON. ANY OTHER COMMENTS? MR. HARRISON, CAN YOU PLEASE RESTATE THE MOTION?

MR. HARRISON: YES. THE MOTION IS TO APPROVE FUNDING FOR APPLICATIONS 5426 WITH A REVISED PROPOSAL ALONG THE LINES OF AN EARLY TRANSLATION AWARD AND A BUDGET OF UP TO SIX MILLION.

CHAIRMAN THOMAS: MARIA, PLEASE, ROLL CALL VOTE.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: YES.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: YES.

MS. BONNEVILLE: JACOB LEVIN.

DR. LEVIN: YES.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.
MS. BONNEVILLE: MICHAEL FRIEDMAN.
DR. FRIEDMAN: YES.
MS. BONNEVILLE: LEEZA GIBBONS.
MS. GIBBONS: YES.
MS. BONNEVILLE: MICHAEL GOLDBERG. SAM HAWGOOD.
DR. HAWGOOD: YES.
MS. BONNEVILLE: STEPHEN JUELSGAARD.
DR. JUELSGAARD: YES.
MS. BONNEVILLE: BERT LUBIN.
DR. LUBIN: YES.
MS. BONNEVILLE: MICHAEL MARLETTA. PHIL PIZZO. CARMEN PULIAFITO.
DR. PULIAFITO: YES.
MS. BONNEVILLE: ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.
MS. SAMUELSON: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: JONATHAN SHESTACK.
MR. SHESTACK: YES.
MS. BONNEVILLE: OSWALD STEWARD.
DR. STEWARD: YES, ON THE BASIS OF NEW DATA THAT HAS UNDERGONE SCIENTIFIC REVIEW.

CHAIRMAN THOMAS: IS THERE AN ACRONYM FOR THAT RESPONSE?

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: YES.

CHAIRMAN THOMAS: PASSES. DR. NELSON, CONGRATULATIONS.

(APPLAUSE.)

DR. FEIGAL: AND WHAT WOULD THE CHAIR LIKE NEXT?

CHAIRMAN THOMAS: SO WE HAVE THE TWO OTHER ITEMS THAT WERE REFERRED FOR RE-REVIEW. THEY WERE NOT RECOMMENDED FOR APPROVAL. OUR PROCESS HERE, MR. HARRISON, IS THAT I AM ASKING ARE THERE ANY MEMBERS OF THE BOARD WHO WOULD LIKE TO MAKE A MOTION THAT WE FUND EITHER OF THOSE PROPOSALS; IS THAT CORRECT, MR. HARRISON?

MR. HARRISON: OR PERHAPS, FIRST, EVEN DISCUSS WHETHER THEY SHOULD BE FUNDED. IF THERE'S PROPRIETARY DATA THAT WOULD NEED TO BE DISCUSSED BEFORE TAKING A VOTE ON THE MOTION, WE'D HAVE TO OTHERWISE TABLE IT.

CHAIRMAN THOMAS: OKAY. WELL, I KNOW WITH RESPECT TO ONE OF THE ITEMS, THERE IS PROPRIETARY DATA THAT'S GOING TO BE REQUIRED IN CLOSED SESSION, BUT THAT DOESN'T MEAN WE CAN'T ENTERTAIN A MOTION. IS THERE A MOTION FOR EITHER OF THE TWO?

MS. GIBBONS: THANK YOU. YES. I'D LIKE TO MOVE THAT WE FUND PROPOSAL NO. 05416 THAT CAME BACK FROM THE GROUP, GOT RECOMMENDED AGAIN. THAT'S THE ALZHEIMER'S PROPOSAL.

MR. TORRES: SECOND.

CHAIRMAN THOMAS: MOVED BY MS. GIBBONS, SECONDED BY SENATOR TORRES. MR. HARRISON, I ASSUME THAT WE NEED TO HAVE AS MUCH DISCUSSION APPROPRIATE FOR OPEN SESSION AS POSSIBLE BEFORE WE WOULD TABLE TO GO INTO CLOSED SESSION ON THIS MOTION.

MR. HARRISON: THAT'S CORRECT.

CHAIRMAN THOMAS: SO IT'S MOVED AND SECONDED. DR. FEIGAL, PERHAPS YOU COULD GIVE MORE DETAIL, AND THEN WE CAN PROCEED WITH BOARD DISCUSSION AND PUBLIC COMMENT.

DR. FEIGAL: SO THE DISCUSSION THAT I THINK WE WANT TO TALK ABOUT IS NOT THIS ONE. THE DISCUSSION WE WANT TO TALK ABOUT IS ON 5416. THE BOTTOM LINE FOR THIS ONE WAS -- IGNORE WHAT'S ON YOUR SCREEN BECAUSE IT'S NOT THE RIGHT ONE -- IS THE

ALZHEIMER'S DISEASE PROPOSAL. THAT'S FINE. I CAN JUST TALK VERBALLY.

THE KEY CONCERN FROM THE GRANT REVIEW GROUP REVIEW WAS THAT THE APPLICANT IS USING A LOCAL INJECTION FOR A DIFFUSE DISEASE IN THE BRAIN. THE REVIEWERS DID NOT FEEL THERE WAS COMPELLING DATA FOR NEURON MIGRATION IN THE SUBMITTED MANUSCRIPT. SO THE ISSUE WAS THAT THERE WAS KEY DATA THAT WAS SAID TO BE AVAILABLE IN A MANUSCRIPT. AND SO WE ASKED FOR THAT NEW MANUSCRIPT AND ALSO FOR THE JOURNAL EDITOR COMMENT ON THE INFORMATION ABOUT ITS ABILITY TO BE PUBLISHED.

THIS IS THE MANUSCRIPT THAT WAS SPECIFICALLY REFERENCED AT THE ICOC MEETING THAT PROMPTED THE CALL FOR ADDITIONAL ANALYSIS. THE MANUSCRIPT IS NOT YET ACCEPTED ALTHOUGH IT'S POTENTIALLY ACCEPTABLE AND WILL REQUIRE MAJOR REVISIONS ACCORDING TO THE JOURNAL EDITOR NOTE. IN ADDITION, HOWEVER, THE STUDIES IN THIS MANUSCRIPT USED MOUSE NSC'S, NOT THE HUMAN NSC'S THAT WERE PROPOSED FOR THE DISEASE TEAM AWARD. AND ALTHOUGH THERE IS SOME INDICATION THAT PATHOLOGY IS AFFECTED AT A DISTANCE FROM THE INJECTION SITE IN ONE OF THE FIGURES, THIS IS A THERAPEUTIC GENE-MODIFIED MOUSE NSC, SO IT WAS DIFFICULT FOR THE REVIEWERS TO

EXTRAPOLATE TO A NON-GENE MODIFIED HUMAN NSC.

HOWEVER, THE APPLICANT ALSO PROVIDED ADDITIONAL INFORMATION. IT WASN'T REQUESTED, BUT THEY DID PROVIDE A POSTER FROM THE ALZHEIMER'S MEETING IN VANCOUVER WITH FIGURES THAT ACTUALLY WERE ALREADY CONTAINED AND ASSESSED IN THE GRANT APPLICATION. IN ADDITION, THE APPLICANT PROVIDED UNPUBLISHED DATA OF TWO GRAPHS AND A FIGURE WITH THE FIGURE POTENTIALLY RELEVANT TO THE QUESTION OF HUMAN NSC MIGRATION IN THE TRIPLE TRANSGENIC ALZHEIMER'S DISEASE MOUSE BRAIN, WITH THE CELLS MIGRATING AT LEAST TO REGIONS THAT WERE ADJACENT TO THE HIPPOCAMPUS AND ALONG THE WHITE MATTER TRACKS BORDERING THE HIPPOCAMPUS, BUT THE FIGURE REALLY SHOWED ONLY A VERY SMALL AREA OF THE CORTEX, WHICH IS A SITE OF THE WIDESPREAD DEGENERATION IN ALZHEIMER'S DISEASE, AND IT DID NOT APPEAR TO HAVE THE LABELED CELLS IN THIS REGION.

THE ADDITIONAL CONFIDENTIAL MATERIALS THAT WERE SUBMITTED, AND WE'RE NOT PROVIDING MORE DETAILS BECAUSE THE APPLICANTS MADE A POINT THAT THIS WAS CONFIDENTIAL, WERE IN DIFFERENT DISEASE INDICATIONS AND INVOLVED DIFFERENT ANATOMIC AREAS OF DELIVERY OF THE CELLS. AND THE REVIEWERS DID NOT FEEL THAT THESE ADDITIONAL STUDIES, ALTHOUGH INTERESTING, WERE

RELEVANT TO THE DISEASE PROPOSED FOR STUDY IN THIS APPLICATION, THAT OF ALZHEIMER'S DISEASE.

THE REVIEWERS DID AGREE THAT MOST RESEARCHERS WILL ACKNOWLEDGE THAT NEURAL STEM CELLS CAN MIGRATE IN THE MOUSE, BUT THERE ARE SIGNIFICANT ANATOMIC AND SPATIAL ISSUES IN MOVING FROM A SMALL ANIMAL BRAIN TO A HUMAN BRAIN. CAN THE CELLS MIGRATE AND FORM NEW CIRCUITRY OVER SEVERAL CENTIMETERS? THE REVIEWERS FELT THAT THERE WAS MUCH MORE PLAUSIBILITY FOR USING THESE CELLS -- AND BY THE WAY, THESE ARE THE SAME CELLS THAT ARE BEING USED IN ANOTHER APPROVED AWARD THAT YOU MADE IN JULY -- IN A LOCALIZED DISEASE AND INJURY SUCH AS SPINAL CORD INJURY, WHICH WAS FELT TO BE A MORE FEASIBLE VOLUMETRIC ISSUE.

CHAIRMAN THOMAS: THANK YOU, DR. FEIGAL. COMMENTS BY MEMBERS OF THE BOARD?

MS. GIBBONS: IF I MAY PLEASE, THANK YOU VERY MUCH. YOU GUYS HEARD ME REALLY PUSH FOR THIS LAST TIME. IN THE INTERIM I'VE LOOKED AGAIN AT WHAT I THINK IS REALLY A VERY COMPELLING ARGUMENT. I KNOW THE PREMISE ON THIS RE-REVIEW WAS NEW INFORMATION, BUT I REALLY THOUGHT WE WERE GOOD TO GO AND READY TO VOTE IT THROUGH LAST TIME WITHOUT HAVING HAD ANY NEW INFORMATION BECAUSE WE HAVE TWICE

AS A BOARD SUPPORTED THIS APPROACH BEFORE. THIS IS THE COMPANY IN QUESTION HERE THAT HAS THE MOST EXPERIENCE WITH BRAIN STEM CELLS.

AND I WANT TO REALLY REMIND US OF WHAT THE STUDIES THAT GOT US TO THIS POINT WERE FOR. FIRST OF ALL, WE DO HAVE $240 MILLION BUDGETED. WE ARE STILL BELOW THAT NUMBER IF THAT'S RELEVANT TO ANYBODY IN YOUR DECISIONS.

DR. FEIGAL: JUST SO YOU KNOW, WE'RE 194 MILLION.

MS. GIBBONS: EXCELLENT. AND I BELIEVE THIS ONE IS REQUESTING 20 MILLION, WHICH, BY THE WAY, THE COMPANY IS PREPARED TO MATCH -- PROVIDE MATCHING FUNDS FOR THIS 20 MILLION. SO I THINK THAT'S PERSUASIVE AS WELL.

BUT IN THIS STUDY MICE WERE EXPOSED TO A WATER MAZE, RIGHT? AND AFTER A WHILE THEY MEMORIZED THE ROUTE TO GET OUT. AND THEN THE MICE WERE AGED UP AND THEY WERE GIVEN AN ALZHEIMER'S-LIKE DISEASE AND THEY COULDN'T FOR THE LIFE OF THEM FIGURE OUT HOW TO GET OUT OF THE WATER AMAZE.

SO THEY WERE GIVEN THE INJECTION, AND LO AND BEHOLD, THEY REMEMBERED. THEY REMEMBERED. SO I KNOW THERE'S THIS QUESTION OF LOCALIZED INJECTION AND DO THE CELLS MIGRATE. BUT THESE RESEARCHERS

HAVE SHOWN IN A HUMAN BRAIN AUTOPSY OF A PATIENT THAT HAD BATTEN'S THAT THE CELLS DO MIGRATE. AND THEY'VE ALSO SHOWN CLINICALLY THAT IN OTHER ANIMAL MODELS THAT THE CELLS MIGRATE.

BUT WHAT I'M MORE CONCERNED ABOUT HERE IS PROGRAMMATICALLY, WE KNOW, EVERYBODY SAYS IT'S A HUGE UNMET NEED. WE'RE SO QUEUED UP WITH THIS ONE. WE'RE SO GOOD TO GO. THIS IS A SIXTH LEADING CAUSE OF DEATH, THE ONLY ONE IN THE TOP TEN FOR WHICH THERE IS NOTHING, NOTHING, NOTHING, ZILCH.

I THOUGHT IT WAS REALLY COMPELLING IN OUR BINDERS THAT WE WERE GIVEN A LETTER FROM DON REED. AND I JUST THOUGHT DON SOMETIMES GETS THINGS DOWN TO THE BASICS, AND THIS TO ME REALLY SPOKE TO MY HEART. HE SAYS, "TO THE BEST OF MY KNOWLEDGE, NO SCIENTIST ANYWHERE IS HAVING SUCCESS WITH ALZHEIMER'S DISEASE THERAPY OR PRODUCTS. IT'S LIKE DARKNESS EVERYWHERE EXCEPT PERHAPS FOR THIS PROJECT." AND THEN HE SAYS, "IT IS THE NATURE OF SCIENCE TO BE CAUTIOUS AND CAREFUL, RIGHTLY SO. BUT EVERY ONCE IN A WHILE, WE NEED TO STEP UP TO THE PLATE AND TRY FOR THE HOME RUN. I THINK THIS IS IT."

YOU KNOW, WE NEVER KNOW, AS JEFF OFTEN SAYS, WE DON'T KNOW THE REASON WHY WE DO WHAT WE DO. WE HAVE TO BE AGGRESSIVE ESPECIALLY WITH SOME OF

THESE DISEASES FOR WHICH IT LOOKS SO BLEAK. AND I JUST LIKE, AGAIN, THIS ONE TO ME WASN'T ABOUT THE NEW INFORMATION. I FEEL THAT THEY DID SHOW THAT THERE WAS ENOUGH EVIDENCE FOR REVIEWERS TO -- WE HAD A STANDARD DEVIATION OF 12, YOU GUYS, ON THIS ONE. WE HAD VERY HIGH SCORES IN THE LAST TWO. IN OTHER WORDS, WE HAD SAID GREAT. WE BELIEVE IN THIS. WE'RE SUPPORTING THIS. AND I KNOW DR. FEIGAL EXPLAINED THIS AT THE LAST MEETING, BUT WE DO HAVE THE $20 MILLION IN THE MATCHING FUNDS, AND WE HAVE THESE COLONIES OF MICE THAT ARE READY TO GO THAT IS NO SMALL AND NO -- IT'S A VERY COSTLY SITUATION AS WELL. IT JUST SEEMS LIKE THE TIMING IS RIGHT.

SO I KNOW WE DON'T HAVE TECHNICALLY THE NEW INFORMATION OR IT HASN'T QUALIFIED TO BE CONSIDERED ALTHOUGH I GUESS IT IS POTENTIALLY QUALIFIABLE. I'M NOT EVEN ASKING US TO TALK ABOUT THE NEW INFORMATION. I THINK BASED ON WHAT THIS IS, THAT IT'S CERTAINLY WORTH -- SO BOARD MEMBERS, TALK TO ME ABOUT WHAT YOUR FEELING IS. I THINK IT'S WORTH US VOTING THROUGH.

CHAIRMAN THOMAS: THANK YOU.

DR. PRIETO: I FEEL THAT LEEZA HAS HIT MOST OF WHAT I WANTED TO SAY VERY WELL, BUT I THINK THAT THERE WAS A LARGE DIFFERENCE OF OPINION IN THE

ORIGINAL REVIEW REGARDING THIS AND REGARDING THE SCIENTIFIC VALIDITY OF SOME OF THE POINTS. I UNDERSTAND THE QUESTIONS ABOUT THE ANIMAL MODEL, AND I'VE NEVER BEEN A LAB SCIENTIST, BUT AS A CLINICIAN I CAN SEE -- I'M SURE THERE IS NO IDEAL ANIMAL MODEL FOR ALZHEIMER'S DISEASE. WE'RE JUST NOT GOING TO FIND ONE. BUT WHEN WE LOOK AT THIS PROGRAMMATICALLY, WHICH IS OUR SCOPE OF OPERATION HERE AT THIS BOARD, IF WE BELIEVE THAT THERE IS A POTENTIAL FOR STEM CELL TREATMENT TO HELP ALZHEIMER'S DISEASE, THEN IS THERE A GROUP BETTER POSITIONED TO SUCCEED IN THAT THAN THIS GROUP? AND DO WE HAVE A PROJECT THAT HAS A BETTER CHANCE OF SUCCESS THAN THIS ONE? I THINK NOT.

SO I WOULD VOTE FOR APPROVAL.

MS. GIBBONS: IF I MAY, THANK YOU SO MUCH. ONE OTHER THING. IT WAS ALSO BROUGHT UP IN THE REVIEW OF THIS WHOLE BUSINESS OF LOCALIZED INJECTION AND WHAT IF IT JUST WORKED ON THE HIPPOCAMPUS AND JUST ATTACKED MEMORY AND NOTHING ELSE? OH, MY GOD. WHAT IF IT JUST ATTACKED MEMORY AND NOTHING ELSE? WHAT IF WE REALLY COULD HAVE A BENEFIT IN RECOVERED MEMORY? THAT WOULD BE HUGE NEWS-MAKING, BELL RINGING SUCCESS CELEBRATION ALL AROUND THE MEMORY LOSS WORLD IF WE HAD THAT.

SO I JUST WANTED TO ADD THAT ONE ADDITIONAL POINT, THAT EVEN IF WE ONLY HAD THAT, WOULDN'T THAT BE FANTASTIC?

CHAIRMAN THOMAS: AND I BELIEVE, DR. FEIGAL, I'M ACCURATE IN SAYING THAT THE PRECLINICAL DATA USING LOCALIZED INJECTIONS INTO THE MICE DIRECTLY INTO THE HIPPOCAMPUS DID RESULT IN SOME RESTORATION OF MEMORY; IS THAT CORRECT?

DR. FEIGAL: RIGHT. I'D ALSO LIKE TO MENTION THAT EARLY TRANSLATIONAL AWARD THAT WE KEEP REFERRING TO ACTUALLY DID HAVE LARGE ANIMALS PROPOSED FOR STUDY. AND THAT SEGMENT OF WHAT THEY HAD PROPOSED TO DO HAS NOT YET BEEN DONE.

CHAIRMAN THOMAS: GETTING BACK TO THE POINT MS. GIBBONS JUST MADE AND I ASKED ABOUT, THERE WAS PRECLINICAL DATA SHOWING SOME MEMORY RESTORATION THROUGH THE LOCALIZED INJECTION PROTOCOL. SO I THINK THAT'S AN IMPORTANT POINT TO NOTE FOR THE BOARD.

OTHER COMMENTS BY MEMBERS OF THE BOARD?

DR. HAWGOOD: JUST A CLARIFICATION. ARE THEY CURRENTLY --

CHAIRMAN THOMAS: DEAN HAWGOOD, I BELIEVE THAT WAS THE -- THANK YOU. THAT WAS WELL SAID. IT'S SORT OF THE VAMPIRE. SO OTHER COMMENTS BY

MEMBERS OF THE BOARD?

DR. FRIEDMAN: I HAVE A QUESTION. THERE ARE A COUPLE OF QUESTIONS I'D LIKE TO ASK THAT I THINK WILL PROBABLY BE PROPRIETARY DATA. CAN I ASK IS THE INTENTION TO VOTE NOW, OR IS THE INTENTION TO DISCUSS IT IN -- THANK YOU.

CHAIRMAN THOMAS: YES, THERE ARE SOME PROPRIETARY ITEMS THAT ARE GROUNDS FOR CLOSED SESSION. WE WILL NOT VOTE ON THIS UNTIL AFTER WE COME BACK FROM CLOSED SESSION.

OTHER COMMENTS BY MEMBERS OF THE BOARD? COMMENTS FROM MEMBERS OF THE PUBLIC, PLEASE? AGAIN, CONFINE YOUR COMMENTS. STATE YOUR NAME PLEASE AND THREE MINUTES, IF YOU WOULD. THANK YOU.

MS. GAY: YES. THANK YOU. HELLO. MY NAME IS RUTH GAY. I'M THE DIRECTOR OF PUBLIC POLICY AND ADVOCACY FOR THE ALZHEIMER'S ASSOCIATION NORTHERN CALIFORNIA, NORTHERN NEVADA. AND I'M HERE TODAY. I'VE BEEN WORKING WITH ALZHEIMER'S DISEASE FOR ABOUT 27 YEARS. I STARTED AT A TIME WHEN I WAS FAIRLY YOUNG, AND THEY STILL CALLED IT SENILE DEMENTIA AND CHRONIC SENILITY AND ORGANIC BRAIN SYNDROME, AND OTHER THINGS.

JUST TO ADD TO SOME OF THE STATISTICS THAT MS. GIBBONS PUT OUT, LET ME JUST SAY THAT WHEN WE

START TALKING ABOUT NUMBERS RIGHT NOW, 5.4 MILLION AMERICANS, 16.2 MILLION UNPAID CAREGIVERS, EVERY DAY 10,000 AMERICANS TURN 65, AND ONE IN EIGHT WILL BE AFFECTED BY THIS DISEASE.

I WAS GOING TO TALK TODAY A LITTLE BIT ABOUT THE DIRECTIONS WE'RE GOING, AND WE'RE BUILDING A POLICY. WE'RE BETTER AT DIAGNOSIS. WE'RE BETTER AT IDENTIFYING. WE'RE WORKING TOWARDS MUCH BETTER TREATMENTS. AND YET TODAY, AFTER I HAD WRITTEN MY WHOLE TOPIC, A GENTLEMAN WALKED INTO MY OFFICE. AND I WAS RUSHING TODAY. HIS NAME IS LEE FOR THE RECORD. HE IS 57 YEARS OLD. HE IS A PRIEST. HE'S A MARRIAGE AND FAMILY THERAPIST. AND HE HAD BEEN DIAGNOSED WITH ALZHEIMER'S DISEASE. AND TO BE HONEST WITH YOU, I HAD NO NEW TREATMENTS TO TALK TO HIM ABOUT THAT I DIDN'T HAVE 27 YEARS AGO. I CAN TALK ABOUT SUPPORT, I CAN TALK ABOUT PLANNING, I CAN TALK ABOUT GETTING INVOLVED WITH COUNSELING, I CAN TALK ABOUT PLANNING FOR THE FUTURE. AND I CAN'T TALK TO HIM ABOUT WHAT CAN WE DO TO CHANGE THE COURSE OF THIS FOR YOU.

WE'RE DEVELOPING A NATIONAL PLAN FOR ALZHEIMER'S DISEASE. WE HAVE A STATE PLAN IN CALIFORNIA. WE'RE PROUD TO FUND RESEARCH AT THE HIGHEST LEVEL AS A PRIVATE FUNDER. AND YET THE

DISEASES THAT ARE BEING FUNDED RIGHT NOW ARE LOOKING AT REDUCTIONS IN DISEASE WHILE ALZHEIMER'S DISEASE DEATHS GO UP EVERY SINGLE DAY. I DON'T KNOW IF THIS RESEARCH STUDY WILL BE THE DISEASE ALTERING TREATMENT OF THE FUTURE. I DO KNOW THAT WE AS THE ALZHEIMER'S ASSOCIATION RESPECT THE STEM CELL WORK. WE RESPECT THE WORK OF THIS COMMITTEE, AND WE HOPE THAT YOU WILL PUT DISEASES LIKE ALZHEIMER'S ON THE FOREFRONT OF YOUR RESEARCH EFFORTS BECAUSE THERE ARE PEOPLE OUT THERE THAT WOULD DO ANYTHING TO CHANGE THE COURSE OF THIS DISEASE. THANK YOU.

CHAIRMAN THOMAS: THANK YOU.

MR. SMITH: RICHARD SMITH. THANK YOU, MR. CHAIRMAN, MEMBERS OF THE BOARD, MS. GIBBONS PARTICULARLY FOR INTRODUCING THIS MOTION. I'VE DONE A LOT OF DANGEROUS AND FRIGHTENING THINGS IN MY LIFE. I FLEW AIRCRAFT CARRIERS OFF THE U.S. KITTY HAWK. AND 14 YEARS AGO I BECAME A CAREGIVER FOR MY WIFE AT AGE 51. SHE WAS DIAGNOSED WITH ALZHEIMER'S. SHE DIED FOUR YEARS AGO UNTREATED FOR THE DISEASE.

I HAVE TWO DAUGHTERS, ONE OF THEM 40 YEARS OLD, THE OTHER ONE 39. MY OLDEST DAUGHTER CELEBRATED HER BIRTHDAY JUST A MONTH AGO. AND WHEN I WAS 40, SHE WAS 15. AND I SAID, "YOU KNOW WHAT," SHE SAID, "DAD, YOU'RE REALLY OLD." I SAID, "HONEY,

WHEN YOU'RE 50, I'M GOING TO BE 75." THAT'S NOT SO BIG A DIFFERENCE AS 40 AND 15. WELL, AT HER BIRTHDAY THIS YEAR, SHE SAID, "DAD, YOU KNOW, REMEMBER WHEN YOU TOLD ME WHEN I'M 50, YOU'RE GOING TO BE 75?" I SAID YEAH. SHE SAID, "WELL, I HOPE I DON'T HAVE ALZHEIMER'S, SO WE CAN THROW A REALLY BIG PARTY."

YOU HAVE THE POWER TO MAKE A DIFFERENCE IN THE COURSE OF THIS DISEASE. YOU HAVE THE POWER TO VOTE YES. THERE ARE NO SOLUTIONS. WHEN I REACH 85, I HAVE A 50-PERCENT CHANCE OF GETTING THE DISEASE. MY DAUGHTERS HAVE A 50-PERCENT CHANCE TODAY. PLEASE SUPPORT THIS ISSUE. THANK YOU.

DR. CAPELA: GOOD EVENING AND THANK YOU FOR THE OPPORTUNITY TO ADDRESS THE BOARD. MY NAME IS ALEXANDRA CAPELA, AND I'M A SENIOR SCIENTIST AT STEM CELLS, AND I'M THE PI ON THIS GRANT PROPOSAL. AND JOINING ME IS DR. FRANK LAFERLA, OUR CO-PI.

SO LAST YEAR WE APPROACHED CIRM WITH A CONCEPT AND WITH A RATIONALE AND A ROAD MAP TO TRANSLATE VERY PROMISING PRECLINICAL DATA INTO USING NEURAL STEM CELLS INTO THE CLINIC FOR PATIENTS WITH ALZHEIMER'S DISEASE. CIRM BELIEVED IN OUR APPROACH, BELIEVED IN OUR TEAM, AND EVENTUALLY FUNDED OUR PLANNING GRANT.

THIS SIGNALED TO US A VERY IMPORTANT VOTE OF CONFIDENCE REGARDING CIRM'S VIEW OF THE BASIC PREMISE OF OUR GRANT. BUT AS OF YESTERDAY, WE UNDERSTAND THAT CIRM AND THE REVIEWERS NOW HOLD, AND I QUOTE, "THERE IS MUCH MORE PLAUSIBILITY FOR USING THESE CELLS IN A LOCALIZED DISEASE INJURY SUCH AS THE SPINAL CORD," END OF QUOTE. IN ESSENCE, IT NOW SEEMS THAT CIRM HAS LOST BELIEF IN A STEM CELL APPROACH FOR ALZHEIMER'S DISEASE, A POSITION THAT IS BEING ADOPTED WITHOUT THE BENEFIT OF ANY HUMAN DATA.

WE ARE TRULY AT A CROSSROADS REGARDING THERAPY FOR ALZHEIMER'S DISEASE. THE TYPES OF THERAPIES THAT -- THE MAJOR STRATEGIES BEING UTILIZED TO REDUCE AMYLOID BURN HAVE YET TO SHOW DISEASE-MODIFYING RESULTS THAT WE HAVE HOPED FOR FOR SO LONG. AND I, AS A SCIENTIST DOING RESEARCH IN NEURODEGENERATIVE DISEASES, REALIZE THAT WE CANNOT AFFORD TO IGNORE ALTERNATIVE APPROACHES, PARTICULARLY APPROACHES THAT ARE BACKED BY COMPELLING PRECLINICAL DATA SUCH AS OUR OWN.

SO I URGE THE ICOC TO APPROVE FUNDING OF OUR GRANT WITH A TEAM THAT TRANSLATED LAB DISCOVERIES WITH THE HUMAN NEURAL STEM CELL IN NOT JUST ONE, BUT FOUR SUCCESSFUL CLINICAL TRIALS. WE HAVE THE EXPERTISE AND AN INTERNATIONALLY RECOGNIZED

TEAM SET UP WITH EXPERTS AT STEM CELLS, INC. AND AT UCI. AND WE ARE VERY COMMITTED IN THIS MISSION ON BEHALF OF CURRENT AND FUTURE ALZHEIMER'S PATIENTS AS WELL AS THEIR CAREGIVERS. SO WE ASK THE ICOC TO BE BOLD IN THE FACE OF SUCH A SERIOUS DISEASE AND ENABLE US TO FOLLOW OUR DATA INTO HUMAN TESTING, WHICH IS WHERE ULTIMATELY WE WILL HAVE ANSWERS. THANK YOU VERY MUCH FOR YOUR ATTENTION.

CHAIRMAN THOMAS: THANK YOU.

DR. LA FERLA: THANK YOU. MY NAME IS FRANK LAFERLA. AND I FIRST WANT TO THANK THE ICOC AND CIRM STAFF FOR CONSIDERING INVESTING IN STEM CELL THERAPY AS A POTENTIAL WAY OF IMPROVING THE MEMORY OF THE 5.4 MILLION AMERICANS, INCLUDING THE 600,000 CALIFORNIANS, THAT ARE AFFLICTED WITH THIS PARTICULAR AND DEVASTATING DISEASE.

I JUST WANT TO MAKE ONE BRIEF COMMENT ABOUT THE LARGE ANIMAL STUDIES. AND I WANT TO POINT OUT THAT I THINK IT'S FAIR TO SAY THAT WE RECEIVED A LITTLE BIT OF A MIXED SIGNAL FROM CIRM REGARDING THE UTILITY OF LARGE ANIMAL MODELS. OUR EARLY TRANSLATION GRANT ACTUALLY DOES INCLUDE A SIGNIFICANT DEVOTION OF THAT STUDY TO LARGE ANIMAL STUDIES, AND WE'VE BEEN ENCOURAGED TO MOVE AWAY FROM THAT. AS A MATTER OF FACT, THAT'S WHY WE ACTUALLY

SLASHED THAT BUDGET FROM $300,000 TO $200,000.

NEVERTHELESS, I WANT TO CEDE MY TIME ACTUALLY TO A PATIENT ADVOCATE WHO COULDN'T BE HERE TONIGHT, AND THAT'S BARRY PETERSON, WHO MANY OF YOU KNOW IS A CBS NEWS CORRESPONDENT, AND HE GAVE US PERMISSION TO ACTUALLY PLAY ONE OF HIS VIDEOS SO THAT HE CAN MAKE A VERY IMPORTANT POINT HERE.

(VIDEO WAS SHOWN, NOT REPORTED, NOR HEREIN TRANSCRIBED.)

DR. LA FERLA: SO JUST THE LAST COMMENT THAT HE MADE IN AN E-MAIL, AND THAT WAS THERE'S SO MUCH NEED AND SO LITTLE TO OFFER THE PEOPLE. SO THANK YOU VERY MUCH.

CHAIRMAN THOMAS: THANK YOU. NEXT PLEASE.

MR. SCHNEIDER: I'M LON SCHNEIDER. I'M A PROFESSOR AT THE UNIVERSITY OF SOUTHERN CALIFORNIA AND A CO-INVESTIGATOR ON ANOTHER GRANT. I DON'T WANT -- I JUST WANT TO ALERT THE BOARD THAT WE ALSO WILL AND WE DO HAVE -- WE HAVE INVITED A NUMBER OF OUR PATIENTS, PARTICIPANTS, SUPPORTERS, SOME OF WHOM HAVE ILLNESS, UP TO TESTIFY AS WELL. AND I JUST WANTED TO SAY THAT. IT'S LATE. IT'S GETTING ON IN TIME, AND I JUST WANTED TO LET YOU KNOW THAT WE WOULD ALSO BE TALKING ABOUT THE DIFFICULTIES WITH ALZHEIMER'S DISEASE.

CHAIRMAN THOMAS: THANK YOU. NEXT, PLEASE.

DR. HUHN: I'M DR. STEPHEN HUHN. I'M A VICE PRESIDENT FOR THE CNS PROGRAM AT STEM CELLS, INCORPORATED. THANK YOU FOR THE OPPORTUNITY TO SPEAK, AND I'LL BE VERY BRIEF.

NOTWITHSTANDING THE GRANTS WORKING GROUP MOST RECENT RECOMMENDATIONS, I'D LIKE TO STRONGLY URGE THE ICOC TO APPROVE FUNDING FOR THE GRANT APPLICATION FOR TWO REASONS. THIS IS THE ONLY DISEASE TEAM THAT'S CURRENTLY WITHIN CIRM'S GRASP TO TEST THE POTENTIAL OF STEM CELL TRANSPLANTATION FOR ALZHEIMER'S, A DISEASE THAT WE ALL CAN NOW RECOGNIZE WITH HUGE UNMET NEED. WE ALL ALSO UNDERSTAND THAT PRECLINICAL DATA IS NEVER WITHOUT GAPS, BUT I THINK WE OWE TO IT OUR PATIENTS AND THEIR FAMILIES TO EXPLORE ALL AVENUES OF RESEARCH THAT MIGHT YIELD MEANINGFUL RESULTS AND IMPACT THIS DEVASTATING DISEASE.

WE BELIEVE THAT THE RECENT AND WELL-PUBLICIZED FAILURES OF PHARMACEUTICAL APPROACHES FURTHER UNDERSCORES THE IMPORTANCE OF INVESTIGATING UNEXPLORED PATHWAYS THAT'S REPRESENTED BY OUR PRECLINICAL DATA, RESULTS WHICH, IF REPLICATED IN HUMAN PATIENTS, WOULD FAR SURPASS THE

BENEFIT OF ANY CURRENT THERAPY FOR ALZHEIMER'S.

SECONDLY, WE RESPECTFULLY DISAGREE WITH THE OPINION OF THE GRANTS WORKING GROUP THAT WE HAVE NOT PRESENTED A COMPELLING RATIONALE TO SUPPORT THIS APPLICATION. I'D LIKE TO POINT OUT THAT WE'VE ADDRESSED AT CONSIDERABLE LENGTH AND EFFORT THE REVIEWERS' CONCERNS ABOUT A LOCAL APPROACH TO DIFFUSE DISORDER AS WELL AS THE MIGRATORY PROPERTIES OF THE HUMAN STEM CELL BOTH IN ANIMAL DATA AND HUMAN DATA.

IT'S IMPORTANT ALSO TO EMPHASIZE THAT THESE SAME CELLS ARE NOW IN CLINICAL TRIALS AND SHOWING CLINICAL EFFECTS IN BOTH BRAIN AND SPINAL CORD DISORDERS. OUR TEAM, WHICH INCLUDES INTERNATIONALLY RECOGNIZED EXPERTS WHO ARE OBJECTIVE, REMAINS CONVINCED THAT THE COMPELLING NATURE OF THE DATA AND THE VALIDITY OF OUR CLINICAL APPROACH. WITH THE SUPPORT OF THE ICOC, WE'LL MAKE THE CASE WITHIN FOUR YEARS TO THE FDA TO INITIATE A HUMAN STUDY AND BEGIN TESTING THIS IN PATIENTS.

I'D LIKE TO CLOSE WITH THAT WHEN I WAS 27, I BECAME A PHYSICIAN. I SWORE AN OATH NOT TO CURE, BUT TO RELIEVE THE SUFFERING OF PATIENTS. THIS TYPE OF RESEARCH GOES A LONG WAYS TOWARD HELPING FULFILL THAT OATH. AND ALTHOUGH I'M AN EMPLOYEE OF A

BIOTECH COMPANY, I'M A PHYSICIAN FIRST. BREAKTHROUGHS IN MEDICINE OFTEN COME FROM UNTESTED AND CONTROVERSIAL AREAS. AND ALZHEIMER'S IS CERTAINLY IN NEED OF A BREAKTHROUGH. THANK YOU.

CHAIRMAN THOMAS: THANK YOU.

MR. MC GLYNN: GOOD EVENING. MY NAME IS MARTIN MCGLYNN. I'M THE PRESIDENT AND CEO OF STEM CELLS, INC. ON BEHALF OF THE STEM CELLS BOARD, I WISH TO THANK THE ICOC AND CIRM AND ITS HARDWORKING STAFF FOR ALL THE CONSIDERATION THAT THEY HAVE GIVEN TO OUR DISEASE TEAM APPLICATION, WHOSE FOCUS IS TO STUDY THE POTENTIAL OF NEURAL STEM CELLS TO IMPROVE MEMORY IN ALZHEIMER'S PATIENTS. WE'VE ALREADY SHOWN THAT THE CELLS DO JUST THAT IN A SIGNIFICANT WAY IN TWO RELEVANT ALZHEIMER'S MOUSE MODELS.

NOW, WE DO REALIZE THAT THE ICOC FACES DIFFICULT CHOICES OF HOW BEST TO SPEND STATE MONEY. WE HOPE THAT THE STATEMENTS MADE HERE TODAY AND AT THE LAST ICOC MEETING AND IN OUR VARIOUS PETITIONS TO THE CIRM HAVE MADE IT ABUNDANTLY CLEAR THAT WE AS A COMPANY REMAIN UNWAVERING IN OUR COMMITMENT TO DEVELOPING OUR PROPRIETARY NEURAL STEM CELLS AS A POTENTIAL TREATMENT FOR A WIDE RANGE OF DISEASES AND DISORDERS OF THE CENTRAL NERVOUS SYSTEM.

WHATEVER DIFFERENCES OF OPINION WE MAY

STILL HAVE WITH THE INDIVIDUALS SERVING ON THE GRANTS WORKING GROUP, WE HOPE THAT THE ICOC NOW APPRECIATES THAT OUR TEAM, WHICH INCLUDES MANY EXPERTS IN THE ALZHEIMER'S FIELD AND WHICH ALREADY HOLDS SUCCESSFUL HUMAN CLINICAL DATA FROM OTHER DIFFUSE DISEASES AFFECTING THE BRAIN, SUCH AS BATTEN'S DISEASE, STANDS READY TO TEST THESE CELLS IN A CLINICAL STUDY TO SEE IF THEY CAN BE ANOTHER TOOL IN THE STATE'S ARMAMENTARIUM AGAINST ALZHEIMER'S, ONE OF THE MOST CRIPPLING DISEASES FACING OUR AGING POPULATIONS.

THE APPLICATION NOW BEFORE THE ICOC PRESENTS A TRULY UNIQUE OPPORTUNITY, BUT IT HAS A RELATIVELY SHORT HALF-LIFE. A WORLD-CLASS TEAM WHICH IS EXPERIENCED IN THIS FIELD OF ENDEAVOR IS IN PLACE. THE PROPRIETARY GMP SEED STOCK CELLS ARE IN THE FREEZERS. AND THE MICE ARE AGING AS I SPEAK AND READY TO BE TRANSPLANTED. WITHOUT IMMEDIATE CIRM FUNDING FOR THIS PROGRAM, OUR COMPANY WILL LIKELY NEED TO MAKE SOME VERY DIFFICULT CHOICES, WHETHER TO FUND IND-ENABLING STUDIES IN ALZHEIMER'S DISEASE OR TO RESERVE SCARCE RESOURCES TO FUND CLINICAL STUDIES THAT ARE ALREADY IN PROGRESS.

PERSONALLY, PERSONALLY I HOPE WE DON'T HAVE TO FACE THAT CHOICE. I ALSO PERSONALLY BELIEVE

THAT THE DATA WE HAVE IN OUR POSSESSION, BOTH PRECLINICAL AND CLINICAL, MAKES A COMPELLING ARGUMENT IN FAVOR OF GOING FORWARD TO TEST THIS GROUNDBREAKING TECHNOLOGY IN ALZHEIMER'S PATIENTS.

IN CONCLUSION, I WOULD LIKE TO LEAVE YOU WITH A QUOTE FROM ALBERT EINSTEIN. "STRANGE IS OUR SITUATION HERE UPON EARTH. EACH OF US COMES FOR A SHORT VISIT NOT KNOWING WHY, YET SOMETIMES SEEMING TO DEFINE A PURPOSE. FROM THE STANDPOINT OF DAILY LIFE, HOWEVER, THERE IS ONE THING WE DO KNOW. THAT MAN IS HERE FOR THE SAKE OF OTHER MEN." THANK YOU.

CHAIRMAN THOMAS: THANK YOU. MR. KLEIN, WELCOME.

MR. KLEIN: BOB KLEIN. AS YOU KNOW, THIS IS ONLY THE SECOND TIME I'VE APPEARED BEFORE THE BOARD IN THE YEAR AND A HALF SINCE I STEPPED DOWN. I APPEAR TODAY FOR A VERY UNIQUE COMBINATION OF REASONS. FOR IN THE SEVEN YEARS I SERVED ON THE BOARD AND THE 20 DIFFERENT PEER REVIEW GROUPS I SERVED ON, THIS IS THE BEST SHOT THAT I SAW FOR ADVANCING ALZHEIMER'S RESEARCH.

HAVING SAT ON TWO DIFFERENT PEER REVIEWS THAT REVIEWED THE SPECIFIC FUNDAMENTAL DESIGNS OF THIS PARTICULAR GRANT WHERE THERE ARE TWO FOCAL IMPLANTATIONS IN THE TWO HEMISPHERES OF THE

HIPPOCAMPUS, BOTH OF THE PEER REVIEWS THAT I SAT ON REVIEWED THE QUESTION OF MIGRATION, FOUND IT WAS NOT ESSENTIAL, THEY WERE GOING TO FOCUS ON MEMORY, THEY WERE GOING TO FOCUS ON THESE TWO FOCAL IMPLANTS IN THE HIPPOCAMPUS, AND BOTH OF THEM GAVE A VERY GOOD SCORE TO THIS GRANT.

WHAT WE HAVE HERE IS A DISAGREEMENT BETWEEN THREE DIFFERENT PEER REVIEWS. THOSE TWO REVIEWS WERE NOT SPLIT. THE SCIENTISTS WERE IN AGREEMENT. THIS REVIEW HAS A HUGE SPLIT, A STANDARD DEVIATION OF 12, WITH SOME PEOPLE WANTING TO FUND AND SOME PEOPLE NOT WANTING TO FUND. BUT AS DR. PIZZO SAID IN THE LAST SESSION IN A GENERAL DISCUSSION OF PEER REVIEW, IF YOU HAVE TWO OR THREE PEOPLE THAT PUT A VERY LOW SCORE ON IT, AND YOU HAVE SOME RECUSALS, YOU DISTORT THE WHOLE FUNDING CURVE.

WHAT WE HAVE HERE IS THE BEST COMPANY IN THE UNITED STATES WITH THE MOST CLINICAL EXPERIENCE IN THE BRAIN WITH TWO DIFFERENT CLINICAL TRIALS THAT HAVE DIRECTLY APPLICABLE EVIDENCE, INCLUDING AN AUTOPSY FROM BATTEN'S TWO AND A HALF YEARS AFTER TRANSPLANT, THAT SHOWS MAJOR MIGRATION GREATER THAN THE ENTIRE RANGE OF THE HIPPOCAMPUS IN THE AREA AROUND THE HIPPOCAMPUS. THAT'S A HUMAN AUTOPSY OF A HUMAN CELL IN BATTEN'S DISEASE IN THE BRAIN.

WE HAVE MOUSE DATA THAT CORRELATES TO THAT. UNTIL WE DO A HUMAN TRIAL, WE WON'T GET BETTER EVIDENCE. THIS IS A PROGRAMMATIC AREA WHERE WE HAVE NO DISEASE TEAM APPROPRIATION. UNLESS WE IN A RISK BALANCE LOOK AT THIS PROGRAM AREA AFTER SEVEN YEARS AND SAY THIS IS OUR BEST SHOT, WE HAVE HAD DR. LAFERLA PERFORM, BE VERY HIDE GRADED, WE CAN SEE PUBLISHED STUDIES ON STEM CELL, INC.'S PERFORMANCE, TWO COMPLETED CLINICAL STUDIES IN THE BRAIN WITH NEURAL STEM CELLS, WHAT BETTER SHOT, WHAT BETTER TIME, WHAT TEAM HAS A BETTER CHANCE?

WE HAVE AN OPPORTUNITY HERE TO MOVE SCIENCE FORWARD. AS LEEZA GIBBONS SAYS, CURING OR ADDRESSING OR MITIGATING THE MEMORY ISSUES DO NOT CURE THE WHOLE DISEASE. THEY DO NOT DEAL WITH THE WHOLE BRAIN. BUT THE FDA IS MORE LIKELY TO APPROVE A FOCUSED APPROACH IN THE HIPPOCAMPUS THAN MULTIPLE INSERTIONS AND TRANSPLANTATIONS IN MULTIPLE PARTS OF THE BRAIN. THIS IS $20 MILLION OF COMPANY MONEY BETTING ON THEIR SCIENCE. THIS IS NOT A FREE RIDE. THIS IS A SITUATION WHERE THE BEST COMPANY WITH THE MOST EXPERIENCE HAS LOOKED AT THE DATA AND SAID THIS IS THE TIME TO MAKE A COMMITMENT. 20 MILLION OF MATCHING FUNDS, 20 MILLION OF OUR FUNDS, SEVEN YEARS, THE BEST SHOT ON GOAL. I HOPE YOU CONCUR.

THANK YOU.

CHAIRMAN THOMAS: THANK YOU. FURTHER COMMENTS BY MEMBERS OF THE PUBLIC? HEARING NONE. OKAY. SO WITH RESPECT TO THIS MOTION, WE'VE HAD BOARD DISCUSSION AND PUBLIC COMMENT, WE ARE GOING TO ADDRESS THIS MOTION IN CLOSED SESSION. SO THAT WILL WRAP THAT UP.

NOW, WITH RESPECT TO THE REMAINING PROJECT THAT WAS REFERRED FOR RE-REVIEW, DO WE HEAR A MOTION THAT WE FUND THAT PROJECT? JUST TO BE CLEAR ON THIS, ALAN, DO YOU WANT TO JUST RESTATE WHICH PROJECT THIS IS?

DR. FEIGAL: THIS IS THE BREAST CANCER PROJECT WITH MONOCLONAL ANTIBODY TARGETING THE CANCER STEM CELL.

MS. GIBBONS: MY QUESTION WAS WHILE I DO THINK THERE WAS SOME BOARD MEMBERS THAT HAD -- THAT WANTED MORE INFORMATION ON WHATEVER MAY BE PROPRIETARY ABOUT THIS IN CLOSED SESSION, DO WE NEED TO DEFER A VOTE UNTIL WE HEAR THAT INFORMATION?

CHAIRMAN THOMAS: YES.

MS. GIBBONS: WE DO. GOT IT.

CHAIRMAN THOMAS: OKAY. GETTING BACK TO THIS OTHER PROJECT HERE, DO WE HEAR A MOTION TO FUND THIS PROJECT? OKAY. HEARING NONE, MR. HARRISON,

WITH RESPECT TO PARTICIPANTS IN THE AUDIENCE WHO MAY WISH TO GIVE PUBLIC COMMENT, AT WHAT POINT WOULD THAT BE APPROPRIATE GIVEN THAT WE HAVE NO MOTION TO FUND?

MR. HARRISON: TYPICALLY IT WOULD COME BEFORE A VOTE TO CLOSE FUNDING FOR TIER III.

CHAIRMAN THOMAS: OKAY. SO DO WE HAVE MEMBERS OF THE PUBLIC HERE? WE'RE NOT AT THAT POINT YET. WE DO HAVE MEMBERS. WE'RE NOT AT THE POINT THAT MR. HARRISON JUST DESCRIBED. JUST HANG WITH US FOR A BIT HERE.

OKAY. SO THAT FOR THE MOMENT COMPLETES DISCUSSION OF THE BOARD OF THE FIVE RE-REVIEWED PROJECTS.

MS. SAMUELSON: MR. CHAIRMAN, POINT OF ORDER ON THE ALZHEIMER'S PROJECT. THE VOTE WOULD NEED TO COME BACK HERE TO OPEN SESSION, RIGHT?

CHAIRMAN THOMAS: YES. ABSOLUTELY, YES. WE HAVE NOT HAD A VOTE. WE WILL HAVE CLOSED SESSION. AND WE WILL COME BACK AND HAVE THAT, AND WE WILL ALSO BE ADDRESSING TIER III -- LET ME GO ON. I KNOW THAT WE'RE -- HOLD ON ONE SECOND, DR. FEIGAL. THERE ARE, AS WAS NOTED, THERE IS ANOTHER PROJECT THAT HAD ADDITIONAL INFORMATION THAT WAS SUBMITTED, ACTUALLY TWO, CORRECT, NOT EXTRAORDINARY PETITIONS.

THESE WERE WHAT WE WOULD CALL OTHER CORRESPONDENCE THAT WERE RECEIVED.

DO WE HAVE A MOTION TO FUND EITHER OF THOSE? YOU HAVE THOSE IN YOUR PACKET. DR. FEIGAL, COULD YOU JUST IDENTIFY THOSE TWO, PLEASE, FOR THOSE WHO HAVEN'T HAD A CHANCE TO READ IT?

DR. FEIGAL: THE TWO THAT YOU RECEIVED WERE THE PROPOSAL WITH THE BISPECIFIC ANTIBODY DIRECTED TO A TARGET FOR GLIOBLASTOMA AND THE SECOND IS ACTUALLY A PROPOSAL IN ALZHEIMER'S DISEASE WITH A SMALL MOLECULE APPROACH. DO YOU NEED THE NUMBERS?

DR. SAMBRANO: SO IT'S 5410, THAT'S THE ALZHEIMER'S, AND 5373, THAT'S THE BISPECIFIC ANTIBODY.

CHAIRMAN THOMAS: MS. GIBBONS.

MS. GIBBONS: I JUST HAVE A PROCESS QUESTION. WITH THE WAY THESE TWO WERE PRESENTED, IS IT WITHIN OUR PURVIEW TO ACTUALLY VOTE FOR FUNDING, OR ARE THEY OUTSIDE OF THE ACCEPTED PARAMETERS THAT WE HAVE?

CHAIRMAN THOMAS: THESE ACTUALLY ARE PART OF THE TIER III GROUP THAT CURRENTLY ARE NOT RECOMMENDED FOR FUNDING. WE WILL BE ASKING IF THERE ARE ANY MOTIONS TO APPROVE MOVING ANY OF THE TIER III PROJECTS UP TO TIER I, CORRECT, MR. HARRISON?

MR. HARRISON: YES. WE'LL BE ASKING THE BOARD IF ANYONE WOULD LIKE TO MAKE A MOTION TO FUND AN APPLICATION IS THAT CURRENTLY IN TIER III.

CHAIRMAN THOMAS: CORRECT. AND THESE TWO ARE AMONGST THOSE IN TIER III. THEY HAPPEN TO HAVE HAD SOME INFORMATION THAT WAS INCLUDED IN PART OF YOUR PACKET THERE.

SO REPEATING THE QUESTION, IS THERE A MOTION THAT WE MOVE TO FUND EITHER OF THE TWO PROJECTS JUST DESCRIBED BY DR. FEIGAL?

DR. FEIGAL: ACTUALLY TO BE CLEAR, I HAVEN'T DESCRIBED THEM. I JUST TOLD YOU THE TITLE.

CHAIRMAN THOMAS: THANK YOU.

MS. GIBBONS: I'D LIKE TO HEAR MORE ABOUT THE -- I BELIEVE THAT DR. SCHNEIDER AND SOME OTHER PEOPLE ARE HERE. I'D LIKE TO HEAR MORE ABOUT THAT PROPOSAL IF WE COULD. IS THAT ON THE TABLE?

DR. FEIGAL: IF YOU WOULD LIKE THAT, WOULD YOU LIKE TO FIRST HEAR THE SCIENTIFIC OFFICER SUMMARY OF THE PROPOSAL?

CHAIRMAN THOMAS: YES, PLEASE.

DR. PRICE: POINT OF INFORMATION. IF THESE AREN'T EXTRAORDINARY PETITIONS, WHAT ARE THEY? AND WHEN DID THE NEW INFORMATION COME TO US?

CHAIRMAN THOMAS: DR. SAMBRANO, PERHAPS

YOU'D LIKE TO ANSWER THAT QUESTION.

DR. SAMBRANO: SO THE COVER MEMO INDICATES THE DATE THAT THE INFORMATION OR LETTER WAS RECEIVED. SO I THINK THE BOARD WILL CONSIDER A PROCESS BY WHICH THE BOARD INTENDS TO CONSIDER EXTRAORDINARY PETITIONS. SO UNDER THAT POLICY CURRENTLY WE NORMALLY ACCEPT THEM AT THE ICOC MEETING WHEN THE BOARD IS ACTUALLY VOTING ON THEM OR INITIALLY VOTING ON THEM, WHICH WOULD HAVE BEEN THE LAST BOARD MEETING.

SO FOR THESE TWO, THEY CAME IN AFTER THAT BOARD MEETING. WE DIDN'T EXPECT THAT WE WOULD BE AT THIS BOARD MEETING CONSIDERING DISEASE TEAM APPLICATIONS, BUT NEVERTHELESS THEY CAME IN. AND SO AS A PUBLIC BODY, ANY CORRESPONDENCE THAT COMES AND IS ADDRESSED TO THE BOARD WE PROVIDE TO YOU. AND SO IT'S UP TO YOU TO DETERMINE WHAT YOU WISH TO DO WITH THOSE.

DR. PRICE: FOR MY BENEFIT, CAN YOU TELL US WHEN THEY CAME IN SO I DON'T HAVE TO RIFLE THROUGH?

DR. SAMBRANO: AUGUST 23D FOR THE -- THAT WAS 5410. AND AUGUST 29TH FOR THE OTHER ONE. I DON'T HAVE THE MEMO IN FRONT OF ME.

CHAIRMAN THOMAS: ZACH, YOU WANT TO

PROCEED HERE.

DR. SCHEINER: CHAIR THOMAS, MEMBERS OF THE BOARD, I'LL PRESENT APPLICATION 5410 ENTITLED "CIRM DISEASE TEAM TO DEVELOP ALLOPREGNANOLONE FOR PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE." I CAN GIVE YOU A SECOND TO FIND THE REVIEW REPORT IN YOUR BINDERS. AGAIN, IT'S APPLICATION 5410.

MR. TORRES: YOU NEED TO IDENTIFY YOURSELF.

DR. SCHEINER: I'M ZACH SCHEINER. I'M A SCIENCE OFFICER AT CIRM.

THIS APPLICATION IS FOCUSED ON A SMALL MOLECULE THERAPY FOR ALZHEIMER'S DISEASE. SMALL MOLECULE IS ALLOPREGNANOLONE, A STEROID THAT OCCURS NATURALLY IN THE HUMAN BODY AND IS A METABOLITE OF PROGESTERONE.

THE APPLICANT HAS PUBLISHED PRECLINICAL DATA SHOWING THAT ALLOPREGNANOLONE PROMOTES THE GENERATION OF NEW NEURONS AND IMPROVES COGNITIVE FUNCTION IN A MOUSE MODEL OF ALZHEIMER'S.

THE APPLICATION PROPOSES IND-ENABLING PRECLINICAL WORK, IND FILING, AND TWO CLINICAL TRIALS. THE FIRST CLINICAL TRIAL WOULD TEST SAFETY, ESTABLISH DOSING, AND LOOK FOR PRELIMINARY SIGNS OF EFFICACY IN ALZHEIMER'S PATIENTS.

THE SECOND WOULD SEEK TO ESTABLISH PROOF OF CONCEPT FOR ALLOPREGNANOLONE IN A LARGER PLACEBO CONTROLLED TRIAL.

SO I'LL BRIEFLY SUMMARIZE THE STRENGTHS AND WEAKNESSES OF THE PROPOSAL AS IDENTIFIED BY THE GRANTS WORKING GROUP. AND THEN I'D BE HAPPY TO TAKE ANY QUESTIONS ABOUT THAT.

THE MAIN STRENGTHS WERE AS WE'VE HEARD TONIGHT, THE ENORMOUS UNMET MEDICAL NEED REPRESENTED BY ALZHEIMER'S DISEASE, THE APPLICANT'S STRONG PRECLINICAL DATA, AND THE THERAPEUTIC DEVELOPMENT READINESS. SO SPECIFICALLY THAT ALLOPREGNANOLONE HAS ALREADY BEEN TESTED IN HEALTHY HUMAN SUBJECTS AND THE TEAM HAS HELD A PRE-IND MEETING WITH FDA.

THERE WERE REALLY TWO KEY WEAKNESSES IDENTIFIED BY REVIEWERS. AND I'M GOING TO READ THEM TO YOU FROM THE REVIEW SUMMARY. THE FIRST IS IN THE FIRST BULLET UNDER SIGNIFICANCE AND IMPACT. SO THIS READS, THE RESPONSIVENESS OF THIS PROPOSAL TO THE RFA IS MARGINAL. WHILE THE APPLICANT PRESENTS PRECLINICAL DATA DEMONSTRATING THAT ALLOPREGNANOLONE HAS EFFECTS ON NEUROPROGENITOR CELLS, IT IS NOT CLEAR THAT THESE EFFECTS ARE RESPONSIBLE FOR THE COGNITIVE IMPROVEMENT OBSERVED IN RODENT MODELS OF AD. THE PHARMACOLOGICAL TARGET OF ALLOPREGNANOLONE

IS WIDELY EXPRESSED IN THE NERVOUS SYSTEM, AND THUS THE DRUG MAY PRODUCE ITS EFFECTS THROUGH MECHANISMS UNRELATED TO NPC PROLIFERATION AND DIFFERENTIATION. SO THAT WAS A RESPONSIVENESS CRITICISM.

THE SECOND MAIN WEAKNESS IS IN THE FIRST BULLET UNDER PROJECT RATIONALE, WHICH READS, THE SIDE EFFECTS OF SEDATION AND MEMORY IMPAIRMENT OBSERVED IN A PREVIOUS CLINICAL TRIAL OF ALLOPREGNANOLONE ADD SIGNIFICANT RISK TO THE PROJECT. THESE SIDE EFFECTS MAY MAKE IT DIFFICULT TO OBSERVE COGNITIVE IMPROVEMENT IN ALZHEIMER'S DISEASE PATIENTS.

REVIEWERS HAD OTHER CONCERNS ABOUT THE TARGET PRODUCT PROFILE AND INTELLECTUAL PROPERTY PROTECTION FOR ALLOPREGNANOLONE. REALLY THE FIRST TWO CRITICISMS I HIGHLIGHTED WERE THE MAIN DRIVERS OF THE GRANTS WORKING GROUP RECOMMENDATION.

THE APPLICATION WAS DISCUSSED DURING PROGRAMMATIC REVIEW, AND A MOTION WAS MADE TO MOVE IT INTO TIER III, NOT RECOMMENDED FOR FUNDING, WHICH CARRIED.

AS YOU'VE HEARD, ADDITIONAL CORRESPONDENCE WAS FILED BY THE APPLICANT ON AUGUST 23D, AND I'D BE HAPPY TO ANSWER ANY QUESTIONS ABOUT THE PROJECT OR THE REVIEW.

CHAIRMAN THOMAS: THANK YOU, DR. SCHEINER. HAVING HEARD THAT DESCRIPTION, DO WE HAVE A MOTION TO ELEVATE THIS FROM TIER III TO TIER I?

MS. GIBBONS: CAN WE HEAR PUBLIC COMMENT OR NOT BEFORE WE MAKE A MOTION?

CHAIRMAN THOMAS: I THINK WE NEED A MOTION FIRST. BEFORE WE HAVE PUBLIC COMMENT, WE NEED A MOTION.

MS. GIBBONS: I'D REALLY LOVE TO HEAR PUBLIC COMMENT, SO I WILL MOVE THAT WE PLEASE MOVE THIS UP FOR FUNDING.

DR. JUELSGAARD: SECOND.

CHAIRMAN THOMAS: HERE'S WHAT WE'RE GOING TO DO. WE ARE GOING TO BREAK FOR -- BETH NEEDS A BREAK. SHE'S SITTING WITH ACUTE WRITER'S CRAMP. AND WE HAVE A BUFFET DINNER FOR THE BOARD, WHICH I WOULD PLEASE LIKE THE BOARD TO GO HELP THEMSELVES TO AND BRING BACK HERE SO WE CAN CONTINUE WITH A WORKING DINNER. FIRST ORDER OF BUSINESS WILL BE DISCUSSION FROM MEMBERS OF THE BOARD ON THIS, IF ANY, AND THEN PUBLIC COMMENT. SO LET'S TAKE A QUICK BREAK. EVERYBODY PLEASE GET DINNER AND COME BACK AT YOUR EARLIEST CONVENIENCE.

(A RECESS WAS TAKEN.)

CHAIRMAN THOMAS: OKAY. LIKE TO RESUME

THE MEETING. AMY, IS LEEZA OUT THERE? WAIT A MINUTE FOR LEEZA TO COME BACK HERE SINCE SHE INITIATED THE DISCUSSION. OKAY.

SO YOU'VE NOW HEARD DR. SCHEINER'S DESCRIPTION OF THE PROJECT AND THE RECOMMENDATION OF THE GRANTS WORKING GROUP. JAMES, DO WE NEED TO ASK IF THERE'S A MOTION, OR DO WE PROCEED TO PUBLIC COMMENT FIRST? YOU CAN CHEW. WE HAVE A MOTION. THANK YOU.

MR. HARRISON: ANY BOARD MEMBER DISCUSSION?

CHAIRMAN THOMAS: ANY OTHER COMMENTS BY MEMBERS OF THE BOARD IS THE NEXT ORDER HERE.

MR. SHESTACK: CAN I ASK A QUESTION? MAYBE DR. FEIGAL COULD ANSWER. WHAT WAS THE -- SINCE IT WAS PRESENTED NOT AS AN EXTRAORDINARY PETITION, BUT AS WE ARE CALLING -- WHAT'S THE PHRASE?

CHAIRMAN THOMAS: OTHER CORRESPONDENCE.

MR. SHESTACK: -- OTHER CORRESPONDENCE. WHAT FOMENTED THIS PRESENTATION IS OTHER CORRESPONDENCE. WAS THERE ANY NEW INFORMATION OR DATA, OR WAS IT MORE IN THE LINE OF THE EXTRAORDINARY PETITION, WHICH IS TO SAY THAT PEOPLE JUST OBJECTED TO THE REVIEW?

CHAIRMAN THOMAS: DR. FEIGAL.

MR. SHESTACK: WAS THERE SUPPLEMENTAL INFORMATION OR NEW DATA?

DR. FEIGAL: WE DID NOT FEEL THERE WAS NEW INFORMATION THAT ADDRESSED KEY POINTS FROM THE GRANTS REVIEW GROUP. SO WE DIDN'T -- THAT'S OUR INTERNAL SCIENTIFIC OPINION. DOES THAT ANSWER YOUR QUESTION?

CHAIRMAN THOMAS: DR. FRIEDMAN.

DR. FRIEDMAN: ARE WE TALKING ABOUT 05410?

CHAIRMAN THOMAS: YES.

DR. FRIEDMAN: THEN I HAVE A QUESTION, PLEASE, IF I CAN SWALLOW. COULD STAFF EXPLAIN TO ME WHAT THE STEM CELL-RELATED PORTION OF THIS GRANT IS? IT WAS A LITTLE HARD FOR ME TO UNDERSTAND THAT, SO IF YOU WOULD, PLEASE.

DR. TROUNSON: MAYBE, MICHAEL, I CAN TRY. THE REVIEWERS FELT THAT THERE WAS A PROBLEM IN THIS AREA, AND I THINK THAT WAS THE POINT THAT WE WERE TRYING TO STRESS IN THE FIRST INSTANCE, THAT THE REVIEWERS FELT THAT THERE REALLY WASN'T A CONNECTION WITH THE STEM CELL COMPONENT.

THE ARGUMENT THAT THERE IS SOMETHING HAPPENING HERE WITH NEURAL STEM CELL COMPONENT WITH THIS DRUG OR WITH THIS STEROID IS RATHER CONJECTURE.

AND I THINK YOU COULD ARGUE EITHER WAY, THAT IN TERMS OF A NEURAL COMPONENT, THERE SEEMS TO BE SOME ADDITIONAL NEURONAL DEVELOPMENT AS A RESULT OF THE STEROID. BUT THERE'S NO GOOD MECHANISM THAT'S BEEN IDENTIFIED THAT WOULD SAY THAT IT REALLY OPERATES REALLY IN ANY STEM CELL COMPONENT, ALTHOUGH HOW YOU GET MORE NEURAL STEM CELLS IN PLACE WITH IT IS DIFFICULT TO DECIDE.

SO AT THE VERY BEST, IT'S ARGUED EITHER WAY, THAT IT MIGHT BE A COMPONENT THAT HAS SO FAR ESCAPED OUR DETERMINATION MECHANISTICALLY, BUT THERE'S NO OBVIOUS MECHANISM FOR DIRECT IMPACT OF THAT STEROID ON A STEM CELL POPULATION.

DR. FRIEDMAN: AND IF IT'S NOT GETTING INTO COMMERCIAL CONFIDENTIAL INFORMATION OR PROPRIETARY INFORMATION, IS THERE A MORE COMPELLING MECHANISM THAT THE INVESTIGATORS HAVE BEEN ABLE TO IDENTIFY? AGAIN, IF I'M ASKING AN INAPPROPRIATE QUESTION, I DON'T MEAN TO.

DR. SCHEINER: THEY PROPOSE THAT IT DOES ACT ON NEUROPROGENITOR CELLS IN THE RODENT AND HUMAN NEURAL STEM CELLS IN CULTURE. BUT, NO, THE REVIEWERS' MAIN CONCERN IS THAT THIS STEROID OPERATES, ACTS THROUGH A RECEPTOR THAT'S WIDELY EXPRESSED IN THE BRAIN. SO IT COULD BE OPERATING BY

MANY MECHANISMS THAT ARE NOT STEM CELL RELATED.

DR. TROUNSON: THE DRUG IS WIDELY USED. AND BECAUSE IT'S A NATURAL HORMONE, IT'S USED IN A NUMBER OF DIFFERENT SITUATIONS.

CHAIRMAN THOMAS: MS. GIBBONS.

MS. GIBBONS: I DON'T KNOW IF IT'S NEW INFORMATION, TO YOUR POINT, JONATHAN, OR IF IT'S JUST INFORMATION THAT I WAS UNAWARE OF, BUT I'D LIKE TO HEAR IF THERE'S ANYBODY OUT HERE WITH THIS PROPOSAL THAT CAN SPEAK TO THIS ABOUT THIS BEING USED EFFECTIVELY FOR TRAUMATIC BRAIN INJURY THAT MIGHT BE INTERESTING TO DR. FRIEDMAN'S POINT.

DR. SCHEINER: THERE IS CURRENTLY A PHASE II CLINICAL TRIAL THAT'S ENROLLING FOR TRAUMATIC BRAIN INJURY WITH THIS SAME STEROID AND I BELIEVE THE SAME OR VERY SIMILAR FORMULATION. THAT'S AT UC DAVIS.

CHAIRMAN THOMAS: ANY FURTHER DISCUSSION FROM MEMBERS OF THE BOARD? HEARING NONE, LET'S PROCEED TO PUBLIC COMMENT. PLEASE IDENTIFY YOURSELVES, AND REMEMBER THREE MINUTES, PLEASE.

DR. DIAZ BRINTON: THANK YOU AGAIN. MY NAME IS DR. ROBERTA DIAZ BRINTON, AND I'M THE PRINCIPAL INVESTIGATOR ON THE PROPOSAL YOU'RE CURRENTLY CONSIDERING FOR ALLOPREGNANOLONE AS A

REGENERATIVE AGENT FOR ALZHEIMER'S DISEASE.

AND TO THE POINT ABOUT THE MECHANISM OF ACTION, IT IS TRUE THAT THE GABA CHLORIDE CHANNEL COMPLEX IS WIDELY DISTRIBUTED THROUGH THE BRAIN. IT IS ACTUALLY EXPRESSED IN PROGENITOR CELLS, AND WE HAVE SHOWN THROUGH PEER REVIEWED JOURNALS AND IN NIH FUNDED GRANTS THAT THERE'S A SPECIFIC MECHANISM THAT IS UNIQUE TO NEUROPROGENITOR CELLS IN WHICH ALLOPREGNANOLONE IS ABLE TO PROMOTE THE PROLIFERATION OF THIS NEURAL STEM CELL POPULATION.

OTHERS HAVE IDENTIFIED THAT ALLOPREGNANOLONE PROMOTES THE REGENERATION OF WHITE MATTER IN BRAIN. AND WE HAVE EVIDENCE FOR THAT IN OUR MOUSE MODEL OF ALZHEIMER'S DISEASE. AND THE RESTORATION OF LEARNING AND MEMORY CAPACITY IN THESE ANIMALS IS INDICATIVE OF REGENERATION OF NEURONAL CIRCUITRY CONSISTENT WITH A NEUROGENESIS MECHANISM.

SO WE HAVE MULTIPLE PEER REVIEWED EVIDENCE FOR THE REGENERATIVE MECHANISM OF ALLOPREGNANOLONE IN THE BRAIN THAT IS WIDELY ACCEPTED IN THE SCIENTIFIC DISCIPLINE.

I WOULD ALSO MAKE MENTION THAT WE ARE THERAPEUTIC READY WITH ALLOPREGNANOLONE. WE HAVE FDA ACCEPTANCE OF TREATMENT OF INDIVIDUALS IN A MULTIPLE ASCENDING DOSE STUDY FOR ALLOPREGNANOLONE.

THEY WILL ACCEPT EXISTING SAFETY DATA IN HUMANS. SO WE ARE THERAPEUTICALLY READY TO TEST ALLOPREGNANOLONE.

AND WITH RESPECT TO THE SEDATION ISSUE THAT WAS BROUGHT UP, WE ARE USING ONE-TENTH THE DOSE NECESSARY TO INDUCE SEDATION. I WOULD ALSO SAY THAT THE MEMORY COMPONENT OF THIS WILL BE ADDRESSED BY DR. SCHNEIDER, BUT WE MENTIONED 34 TIMES IN OUR PROPOSAL THAT WE WOULD USE A DOSE THAT WAS NOT SEDATIVE. WE HAVE ESTABLISHED THE DOSE RESPONSE RELATIONSHIP AND UNDERSTAND THAT SUBSEDATIVE DOSES THAT DO NOT INDUCE SEDATION ARE NEUROGENIC IN THE BRAIN.

I WOULD ALSO MAKE MENTION THAT WE PROVIDED A COMMERCIALIZATION PLAN FROM OUR COMMERCIAL PARTNERS, SAGE THERAPEUTICS, THAT OUTLINES OUR STRATEGY FOR DEVELOPMENT, COMMERCIALIZATION OF ALLOPREGNANOLONE AS A THERAPEUTIC.

AND WITH REGARD TO THAT, THERE IS NEW DATA ON ALLOPREGNANOLONE AND THE CLINICAL GMP MATERIAL THAT'S AVAILABLE AND THE PURITY AND THE CERTIFICATION OF THE EXISTING GMP MATERIAL THAT DR. GERHARD BAUER WILL SPEAK ABOUT AS WELL AS OUTCOMES FROM A SERENDIPITOUS CLINICAL PATIENT TREATMENT.

SO WE HAVE, I BELIEVE, ADDRESSED THE

ISSUES THAT WERE RAISED BY THE REVIEWERS AND ARE PROCEEDING WITH BEING THERAPEUTIC READY. THE REVIEWERS INDICATED THAT WE WERE THERAPEUTIC READY, AND WE'RE CONTINUING TO ADVANCE OUR THERAPEUTIC READINESS AND ARE READY TO LAUNCH INTO A CLINICAL TRIAL.

AND WITH THAT, I WILL ASK MY CLINICAL COLLEAGUE, DR. LON SCHNEIDER, TO RAPIDLY ADDRESS THE ISSUE AROUND MEMORY.

DR. SCHNEIDER: THANK YOU. HELLO AGAIN. LON SCHNEIDER. I'M FACULTY AT USC, AND MY WORK FOR 25 YEARS HAS BEEN IN DRUG DEVELOPMENT IN ALZHEIMER'S DISEASE. I MAY NOT LOOK IT, BUT I WAS THERE AT THE BEGINNING AND IMPORTANTLY INVOLVED IN THE TEAM THAT BROUGHT ALONG THE FIRST SYMPTOMATIC DRUG, HOWEVER IMPERFECT THE DRUG WAS, COGNEX OR TACRINE. AND MY WORK IS IN DRUG DEVELOPMENT.

I WAS ACTUALLY GRATIFIED BY THE REVIEW WORK GROUP THAT THEY DIDN'T SIGNIFICANTLY QUESTION AND SEEM TO HAVE SUPPORTED OUR DRUG DEVELOPMENT PROGRAM, OUR DOSE FINDING STUDY, AND OUR PROOF OF CONCEPT ALONG WITH BIOMARKERS.

IN THE FEW SECONDS THAT I HAVE HERE, I DID WANT TO ADDRESS THE SECOND MAIN CONCERN THAT THE REVIEWERS SEEMED TO HAVE, THAT OF SEDATION AND

MEMORY IMPAIRMENT. YES, THE DRUG IS ACTIVE AT THE GABA COMPLEX. YES, IN HIGH DOSES IT'S SEDATIVE AND ANXIOLYTIC. AND IN STUDIES AT HIGHER DOSES, IT WILL CAUSE A LEARNING DEFICIT. INSTEAD OF PROXIMATELY, IS HALF A WORD DIFFERENCE FROM PLACEBO OUT OF 12 WORDS. AND THAT IS AN EFFECT THAT LASTS A FAIRLY SHORT AMOUNT OF TIME, FROM ABOUT A HALF AN HOUR TO AN HOUR WITH A SINGLE DOSE.

THE DOSES WE ARE USING IN THE DOSE FINDING STUDY AND THE DOSES, BOTH THAT CAME ABOUT FROM PRECLINICAL MODELS AND FROM OUR SIMULATIONS, ARE DOSES THAT START OUT AT ONE-TENTH OF THE DOSE THAT WAS MINIMALLY SEDATIVE IN HUMANS, AND IT'S FIVE DOSES UP TO ABOUT 75, 80 PERCENT OF THAT. SO I THINK IF THIS HAD BEEN AN NIH STUDY SECTION REVIEW, WE WOULD HAVE GOTTEN THE SCORE THAT WE GOT, WE WOULD HAVE GOTTEN THE COMMENTS, AND WE WOULD HAVE RESUBMITTED AND REVISED ON THE ISSUES THAT THE REVIEWERS WERE CONCERNED ABOUT.

SO I THINK WITH THAT, AND BEING AWARE OF THE TIME, I'D LIKE TO STOP.

DR. DIAZ BRINTON: WE HAVE SEVERAL PATIENT AND CAREGIVERS WHO WOULD LIKE TO ADDRESS THE BOARD. MR. AND MRS. MORALES, IF YOU WOULD.

MS. FRANKLIN: ONE IN EIGHT BABY BOOMERS

WILL GET ALZHEIMER'S. I AM A BABY BOOMER. MY NAME IS SUSAN FRANKLIN, AND I HAVE ALZHEIMER'S DISEASE. I WAS DIAGNOSED AT THE AGE OF 58. I WAS AT THE TOP OF MY CAREER, WORKING AS A REGIONAL NETWORK DIRECTOR FOR A HEALTHCARE COMPANY, NEGOTIATING CONTRACTS WITH PHYSICIAN GROUPS AND HOSPITALS. I AM ALSO A REGISTERED NURSE, AND I HOLD A MASTER'S DEGREE FROM UCLA.

THE BIGGEST IMPACT TO ME AND MY FAMILY IS THAT I CAN NO LONGER WORK OR DRIVE. I HAVE TROUBLE REMEMBERING AND HAVE DIFFICULTY IN FINDING WORDS TO SPEAK. AFTER RECEIVING MY DIAGNOSIS, I CHOSE TO BE AN ADVOCATE FOR THIS DISEASE, AND THAT KEEPS ME AND MY HUSBAND VERY BUSY.

I HAVE BEEN IN TWO CLINICAL STUDIES FOR THIS DISEASE, AND CURRENTLY THERE'S NOTHING TO SLOW OR CURE THIS DEVASTATING DISEASE.

TIME IS RUNNING -- TIME IS RUNNING OUT FOR PERSONS LIKE ME. I AM HERE TO SPEAK FOR THE MILLIONS OF OTHERS THAT CANNOT BE HERE TODAY AND THOSE THAT CANNOT REMEMBER. IT'S URGENT TO TEST NEW THERAPIES, ESPECIALLY LIKE THIS USC CIRM ALLO PROJECT FOR REGENERATING BRAIN AND RESTORING COGNITIVE FUNCTION FOR TREATING ALZHEIMER'S. THANK YOU VERY MUCH. I'M SORRY.

MR. MORALES: MY NAME IS SERGE MORALES, AND MY WIFE IS SUSAN FRANKLIN. THE BIGGEST IMPACT OF HER DIAGNOSIS WAS OBVIOUSLY ACCEPTING THE FACT THAT SHE HAS ALZHEIMER'S. IT'S NOT SOMETHING THAT SOMEONE PLANS ON. AS A RESULT OF HER WORD FINDING AND MEMORY ISSUES, I AM LEARNING TO CONTINUE TO LEARN TO BE MORE PATIENT AND TOLERANT IN THINGS THAT SHE DOES.

BECAUSE SHE'S UNABLE TO READILY RECALL AND SAY THINGS, I AM CONSTANTLY REMINDING MYSELF THAT IT'S THE DISEASE THAT IS AFFECTING HER. WHAT SUSAN PREVIOUSLY DID AND WITHOUT HESITATION HAS NOW BEEN SLOWED DOWN. I HAVE ALSO BECOME MORE VIGILANT OF HER ACTIVITIES AT HOME AND IN PUBLIC.

THROUGH OUR ADVOCACY EFFORTS, WE HAVE BECOME AWARE THAT MORE AND MORE PEOPLE HAVE BEEN DEVELOPING THIS DISEASE. WE HAVE MET PEOPLE IN THEIR LATE 20S, 30S, 40S, AND 50S. IT IS NO LONGER A DISEASE OF THE ELDERLY.

SOME SOBERING STATISTICS SHOW THAT EACH DAY 1232 PEOPLE ARE DIAGNOSED WITH ALZHEIMER'S DISEASE. EACH WEEK 8,634 ARE DIAGNOSED. THIS IN ITSELF TELLS YOU THAT TIME IS RUNNING OUT, AND IT IS EXTREMELY IMPORTANT THAT A CURE BE FOUND. THE NEED TO TEST NEW THERAPIES IS CRITICAL, LIKE THE USC CIRM

ALLO PROJECT FOR REGENERATING THE BRAIN AND RESTORING COGNITIVE FUNCTION FOR TREATING ALZHEIMER'S. THANK YOU.

DR. DIAZ BRINTON: I'VE ASKED TERESA MARQUEZ TO JOIN US. SHE IS A COMMUNITY ORGANIZER IN BOYLE HEIGHTS IN LOS ANGELES AND IS AN ADVISOR TO OUR ALZHEIMER'S DISEASE RESEARCH CENTER.

MS. MARQUEZ: GOOD EVENING. THANK YOU VERY MUCH FOR ALLOWING US TO SPEAK. MY NAME IS TERESA MARQUEZ, AND I AM A COMMUNITY ADVOCATE. AND YOU ARE SAYING WHAT IS A COMMUNITY ADVOCATE DOING HERE? WELL, A FEW MONTHS AGO I GOT A CALL FROM THE COMMUNITY SAYING, "TERRY, THEY'RE CLOSING THE DOORS FOR THE DAYCARE CENTER FOR ALZHEIMER'S PATIENTS." AND THIS IS VERY IMPORTANT IN BOYLE HEIGHTS. IT'S A LOW INCOME COMMUNITY WITH OVER 80,000 IN POPULATION IN A THREE-BY-FIVE MILE RADIUS. AND WE ARE RIGHT NEXT DOOR TO USC ALZHEIMER'S RESEARCH.

ONE OF THE MOST DEVASTATING IS THAT THEY GAVE THEM TWO WEEKS' NOTICE TO GET THE PATIENTS BECAUSE THEY WERE GOING TO CLOSE DOWN THE DAYCARE. I STARTED WORKING ON THAT. I CALLED JOHN PEREZ. I'M AN APPOINTEE DELEGATE, DEMOCRATIC DELEGATE, FROM JOHN PEREZ, SPEAKER OF THE HOUSE IN THE STATE OF CALIFORNIA. AND RIGHT AWAY I STARTED TALKING TO HIM

WHEN HE WAS WORKING ON THE BUDGET. AND HE SAYS, "I'M WORKING ON THE BUDGET RIGHT NOW. I CAN'T TALK TO YOU." WELL, I SAID YOU ARE GOING TO HAVE TO.

WHAT I REALIZED -- AND THAT'S THE WAY I AM. OKAY. WHAT I REALIZE, THAT THERE IS SO MUCH FUNDS BEING TAKEN AWAY FROM THIS DISEASE, WHETHER IT IS DAYCARE OR RESEARCH. AND RIGHT NOW USC HAS OPENED UP THE DOORS FOR THIS COMMUNITY, AND THIS COMMUNITY HAS DEVELOPED A TRUST IN USC THAT IS PHENOMENAL BECAUSE I'VE NEVER SEEN AN HISPANIC COMMUNITY TO OPEN UP AND BE TRUSTFUL WITH USC ALZHEIMER'S RESEARCH. AND WE CANNOT STOP THAT.

I WANT TO SUPPORT FOR YOU TO ALLOW THIS MONEY TO COME TO THIS STUDY BECAUSE OF THE ENORMOUS AMOUNT OF WORK THAT THEY HAVE ALREADY DONE AND THE RESEARCH THEY ALREADY HAVE COMMITTED, AND THE PATIENTS THAT HAVE ALREADY COMMITTED TO THE RESEARCH. I'M ONE OF THOSE PATIENTS TOO EVEN THOUGH I DON'T SUFFER FROM ALZHEIMER'S RIGHT NOW. BUT I WANT TO PLEASE PLEAD WITH YOU THAT IF I HAVE IN MY COMMUNITY ALONE OUT OF SIX COMMUNITIES AROUND USC HAS 80,000 IN POPULATION, ONE OUT OF EIGHT IS 10,000 PEOPLE THAT WILL DEVELOP ALZHEIMER'S. AND I COULD JUST NOT IMAGINE THE COST AND THE DEVASTATING PROCESS ON THIS.

ONE OF THE THINGS IS THAT IN THE LOW-INCOME COMMUNITY, THEY DON'T HAVE THE MONEY FOR HAVING SOMEONE COME AND CARE. ONE OF THE PEOPLE HAVE TO STOP WORKING. IF THEY'RE MAKING 40,000 A YEAR FOR FAMILY, THEY ARE GOING TO BE MAKING 20,000 BECAUSE ONE HAS TO STOP WORKING TO TAKE CARE OF THE PATIENT. THANK YOU.

DR. DIAZ BRINTON: WE HAVE ANOTHER PATIENT AND CAREGIVER, THE BENIZES, MR. AND MRS. BENIZ (PHONETIC), AND MERYL BENIZ WILL SPEAK TO YOU FIRST.

MS. BENIZ: HI. I'M MERYL BENIZ. THANK YOU FOR YOUR TIME TODAY. MY NAME IS MERYL BENIZ, AND I'M 59 YEARS OLD. AND THE FIRST SIGNS OF ALZHEIMER'S APPEARED WHEN I WAS 53. I HAVE NO OTHER HEALTH ISSUES, BUT MY LIFE WAS COMPLETELY CHANGED. PLEASE DO WHAT YOU CAN TO SUPPORT ALZHEIMER'S RESEARCH. THANK YOU.

MR. BENIZ: GOOD EVENING. MY NAME IS CARY BENIZ. AND FIRST LET ME EXPLAIN THAT I AGREED TO TRY TO CONTRIBUTE TO THIS CAUSE AND COME UP HERE TODAY UNDER THE UNDERSTANDING THAT MY WIFE COULD NOT BE HEARING WHAT I AM GOING TO EXPRESS TO YOU BECAUSE, FRANKLY, SHE DOESN'T COMPREHEND THOSE KINDS OF THINGS AND SHE DOESN'T NEED TO SINCE, AS A CAREGIVER, IN THE END THE GOAL IS KEEP THEM HAPPY.

MY WIFE AND I WILL HAVE BEEN MARRIED 30 YEARS NEXT MONTH. ALTHOUGH SHE IS INDEED MY WIFE, MY ROLE HAS NOW CHANGED COMPLETELY TO ONE ALMOST PURELY AS A CAREGIVER. THE HUSBAND-WIFE RELATIONSHIP PRETTY MUCH CEASES TO EXIST.

OF COURSE, IT'S A DEVASTATING DISEASE TO THE PATIENT, AS YOU JUST HEARD MY WIFE, BUT IT'S ALSO DEVASTATING TO THE CAREGIVER AND EVERYONE AROUND THE PATIENT.

MERYL SPENT MOST OF HER CAREER AS AN EXECUTIVE ASSISTANT TO PRESIDENTS OF VARIOUS LARGE CORPORATIONS. AND TO DO THAT, YOU OBVIOUSLY HAD TO BE VERY PROFICIENT AT ORGANIZATIONAL SKILLS, MULTITASKING, ETC. CLEARLY THAT DOESN'T WORK ANYMORE. HER CURRENT SITUATION IS SHE CURRENTLY HAS NO SHORT-TERM MEMORY. SHE HAD TO STOP WORKING AND DRIVING FOUR YEARS AGO. SHE CAN NO LONGER READ A BOOK OR MAGAZINE. THAT WAS HER LOVE. SHE STRUGGLES JUST TO MAKE A SIMPLE PHONE CALL. SHE CAN'T COOK OR DO CHORES OR DO ANYTHING TO MAKE HER FEEL LIKE SHE'S CONTRIBUTING AROUND THE HOME, WHICH IS DIFFICULT FOR HER. SHE HAS NO IDEA WHAT'S GOING ON IN THE WORLD. SHE REALLY DOESN'T UNDERSTAND WHY WE'RE HERE TODAY. SHE REALLY DOESN'T UNDERSTAND WHAT'S GOING ON IN OUR FAMILY.

AND SOON I AND THOSE AROUND HER WILL LOOK AT THIS AS THE GOOD OLD DAYS. IT'S NOT THAT FAR AWAY. WHAT'S THE SITUATION FOR THOSE SUPPORTING MERYL? I BALANCE A FULL-TIME JOB AND AM ALSO HER PRIMARY CAREGIVER. WHEN I'M NOT AT WORK, I'M CONSUMED BY THE CHORES OF THE FAMILY AND THE HOME AND EVERYTHING ELSE YOU HAVE TO DO IN LIFE THAT SHE CAN NO LONGER CONTRIBUTE TO. WHEN I GET HOME AT THE END OF THE DAY, SHE DOESN'T KNOW WHAT SHE DID DURING THE DAY. SHE DOESN'T KNOW WHO SHE TALKED TO. IF I LOOK ON HER CELL PHONE AND FIND OUT SHE TALKED TO SOMEBODY 20 MINUTES AGO, LIKE HER FATHER, SHE HAS NO IDEA WHAT SHE TALKED TO HIM ABOUT. AND SHE DOESN'T KNOW WHAT'S GOING ON IN THE WORLD. SO, FRANKLY, THERE'S NOTHING TO TALK ABOUT.

OUR DAUGHTER'S MOVED BACK HOME FROM GRAD SCHOOL TO BE WITH HER MOTHER FOR AS MUCH TIME AS SHE CAN OF WHAT'S REMAINING. AND WHAT DOES THE FUTURE LOOK LIKE? RELATIVELY SOON, EVERYONE IS DIFFERENT, BUT RELATIVELY SOON, HER LONG-TERM MEMORY WILL ALSO FADE. SHE WON'T KNOW ME, HER FAMILY, HER FRIENDS. YOU ALL KNOW THAT. IT'S HIGHLY UNLIKELY THAT SHE'LL BE AT MY DAUGHTER'S WEDDING, EXTREMELY UNLIKELY SHE'LL GET TO KNOW HER GRANDCHILDREN. AND IN THE END, SHE'LL END UP IN A LONG-TERM CARE FACILITY.

AND, FRANKLY, I'LL BE IN MY EARLY 60S BY THEN AND WITHOUT A LIFE PARTNER, STARTING OVER AGAIN.

ALZHEIMER'S IS A CRUEL DISEASE THAT IS, OF COURSE, DEVASTATING TO THE PATIENT, BUT ALSO TO EVERYONE AROUND THEM. IT'S IMPERATIVE NEW ALZHEIMER'S THERAPIES BE TESTED LIKE THE USC CIRM ALLO PROJECT FOR REGENERATING THE BRAIN AND RESTORING COGNITIVE FUNCTION.

AS YOU'VE HEARD REPEATEDLY, OVER FIVE MILLION PEOPLE IN THE UNITED STATES HAVE THIS AND IT'S GROWING FAST. SO I THANK YOU FOR YOUR TIME, AND I THANK YOU FOR YOUR SUPPORT IN ADDRESSING THIS DEVASTATING DISEASE OF THE FAMILY. THANK YOU.

DR. DIAZ BRINTON: OUR LAST SPEAKER IS DR. GERHARD BAUER FROM UC DAVIS, WHO WILL BE SPEAKING ABOUT THE ALLOPREGNANOLONE.

DR. BAUER: THANK YOU. YOU KNOW ME. IN MY SPARE TIME, I DO NOT DO WHATEVER I DO WITH MY CELLS HERE. I ALSO DEVELOP DRUGS. AND THIS DRUG IS IMPORTANT FOR ME BECAUSE MY FATHER DIED OF ALZHEIMER'S DISEASE. TEN YEARS WORTH OF SUFFERING. I HAVE A 50-PERCENT CHANCE OF GETTING IT. MAYBE I WON'T RECOGNIZE YOU IN A FEW YEARS DOWN THE ROAD; BUT WHILE I DO, I'M GOING TO TELL YOU WHAT I'M ACTUALLY DOING WITH THIS DRUG.

FIRST OF ALL, WE'RE CLINICALLY READY. I MAKE THE FORMULATION. I DEVELOPED IT BECAUSE IT WASN'T HERE BEFORE. THIS DRUG HAD TO BE MADE AVAILABLE TO THE BODY BECAUSE IT'S NOT WATER SOLUBLE. IT WAS ACTUALLY INTENDED FOR TRAUMATIC BRAIN INJURY. WE HAVE NOW A PHASE II CLINICAL STUDY APPROVED BY THE FDA BASED ON THE FORMULATION THAT I DEVELOPED. WHAT DID I DO? I DEVELOPED A CONCENTRATE THAT WE CAN FREEZE, AND THAT CONCENTRATE CAN BE SHIPPED ALL OVER THE PLACE FROZEN BECAUSE IT NOW CAN GO TO THE BATTLEFIELD. THIS IS WHAT IT WAS INTENDED, TO TREAT TRAUMATIC BRAIN INJURY OF SOLDIERS ON THE BATTLEFIELD. IT HAS SIDE EFFECTS AND CAN BE USED TO SAVE PEOPLE.

HERE'S THE ANECDOTE. A FEW DAYS AGO WE WERE CALLED BY MASS GENERAL. THERE WAS A 23-YEAR-OLD, AND THAT 23-YEAR-OLD WAS IN A TERRIBLE ACCIDENT AND HE HAD TRAUMATIC BRAIN INJURY. HE WAS NOT ELIGIBLE FOR THE STUDY BECAUSE HE WAS NOT STOPPING TO SEIZE. YOU KNOW WHAT THAT MEANS? YOU CAN'T STOP SHAKING, AND YOUR BRAIN IS DYING. SO THEY HAD TO SEDATE HIM, AND THE SEDATION IS STRONG LIKE ANESTHESIA, AND THEY SAID HE DOESN'T HAVE ANY TIME TO LIVE ANYMORE.

SO WHAT ARE WE GOING TO DO? THE FAMILY

FOUND OUT THAT DR. ROGOWSKI AT UC DAVIS HAD THIS DRUG AND THAT WE CAN MAKE IT. SO WE WERE ASKED TO QUICKLY HAVE AN FDA EMERGENCY EXCEPTION. GUESS WHAT? WE GOT IT. THE PATIENT IS ALLOWED TO BE TREATED WITH OUR DRUG. SO WE MADE IT. WE MADE IT AND WE MADE IT AT NIGHT. SO OUR STAFF CAME IN, WE DID THE DRUG, WE SENT 16 INFUSION BAGS UP TO MASS GENERAL. ON THURSDAY WE STARTED. PATIENT WAS STILL SEIZING. ON FRIDAY HE STARTED TO RESPOND AND MONDAY HE WOKE UP.

SO IF YOU WANT TO KNOW IF THAT DRUG WORKS, IT DOES. THANK YOU.

CHAIRMAN THOMAS: I BELIEVE THAT CONCLUDES PUBLIC COMMENT. IS THERE FURTHER DISCUSSION BY MEMBERS OF THE BOARD? I THINK WE CAN -- ONE MINUTE. IS THERE ANY OTHER DISCUSSION BY MEMBERS OF THE BOARD ON THIS PARTICULAR ITEM?

DR. JUELSGAARD: EARLY ON IN THIS DISCUSSION, DR. FRIEDMAN ASKED DR. TROUNSON WHETHER THIS REALLY AT THE END OF THE DAY WORKED ON NEURAL STEM CELLS, AND DR. TROUNSON INDICATED THAT THERE WAS SOME QUESTION ABOUT THAT. IN ONE OF THE SLIDES THAT DR. FEIGAL PRESENTED WERE THE GROUPS OF COMPOUNDS, MOLECULES, CELLS THAT WE ARE PREPARED TO SUPPORT. NOT JUST PREPARED TO SUPPORT, BUT WE HAVE

THE AUTHORITY TO SUPPORT. AND I THINK WE JUST NEED TO BE CLEAR IN OUR OWN MINDS WHETHER WHAT'S BEING PROPOSED HERE, THIS PARTICULAR MOLECULE, FALLS WITHIN ONE OF THOSE FOUR DIFFERENT GROUPINGS IN OUR MIND OR NOT. BECAUSE I DON'T THINK WE'RE AT THE END OF THE DAY TO BE FUNDING CLINICAL TRIALS THAT AREN'T STEM CELL RELATED.

AND SO I THINK IT'S IMPORTANT THAT WE FIGURE OUT WHETHER THIS MOLECULE IS IN THAT GROUPING OR NOT.

DR. TROUNSON: IT'S REALLY DIFFICULT TO ANSWER THAT BECAUSE I GUESS THAT YOU ALSO CONSIDER OUR BRIEF TO GO OUT TO PROGENITOR CELLS. SO IS IT POSSIBLE THAT THIS DRUG HAS SOME ROLE IN DRIVING THE PROGENITOR CELL FORMATION OR MULTIPLICATION. IT'S REALLY DIFFICULT TO DECIDE, AND IT'S GONE THROUGH THE PROCESSES INTERNALLY AS IF IT'S SUFFICIENTLY WITHIN THE DEFINITIONS. BUT THE GRANTS WORKING GROUP REALLY DID QUERY THIS PRETTY STRONGLY AND THEN MADE THAT A STRONG COMMENT ON IT.

SO WE THOUGHT THAT WE NEEDED TO PASS THAT ON TO YOU BECAUSE THEY DID QUESTION US ABOUT THIS. AND IT'S ARGUABLY ONE WAY OR THE OTHER IN SOME RESPECTS BECAUSE THE TROUBLE WITH CIRM'S BRIEF IS IT'S PRETTY BROAD. IF YOU SAY STEM CELLS AND

PROGENITOR CELLS, YOU'RE REALLY KIND OF SAYING EVERYTHING EXCEPT THOSE UNDIFFERENTIATED CELLS. IT'S A PRETTY DIFFICULT ONE TO CALL ON WITHOUT KNOWING THE EXACT MECHANISMS.

IF WE KNEW THE EXACT MECHANISMS OF HOW IT'S WORKING, THEN I THINK WE COULD BE MUCH MORE SPECIFIC IN ADDRESSING YOUR QUESTION, BUT WE REALLY ARE NOT WELL INFORMED ABOUT THE EXACT MECHANISM OF HOW THIS STEROID IS ACTING.

DR. JUELSGAARD: I'M STILL A LITTLE, I GUESS, PERPLEXED BECAUSE I HAD UNDERSTOOD, AND PERHAPS WRONGLY, THAT WHAT WE WERE FUNDING WERE PROJECTS THAT FIT WITHIN THOSE FOUR GROUPINGS ON THE ONE SLIDE THAT DR. FEIGAL PRESENTED MUCH EARLIER THIS EVENING. AND IF WE IN OUR OWN MINDS CAN'T BE COMFORTABLE THAT IT FITS WITH ONE OF THOSE GROUPS, THEN WHAT ARE WE TO DO?

DR. TROUNSON: WELL, I THINK IT'S UP TO THE BOARD. WE'RE TRYING TO GIVE YOU AS MUCH INFORMATION AS WE CAN PROVIDE. AND YOU COULD ASK A LOT OF PEOPLE AND MAYBE GET QUITE A VARIETY OF ANSWERS ON THIS, I SUSPECT. SO THE GRANTS WORKING GROUP SCIENTISTS DID QUESTION WHETHER THIS WAS REALLY WORKING ON A STEM CELL POPULATION. AND SO WE BROUGHT THAT TO YOUR ATTENTION BECAUSE THAT'S ONE OF

THE KEY ISSUES IN THEIR MIND.

AS WE SAID, WE USUALLY TRY AND MAKE SURE THAT THEY DO FIT WITHIN THE PROGRAM, SO -- BUT UNTIL YOU ACTUALLY GET THE FULL SCIENTIFIC STUDY SOMETIMES, YOU'RE ALWAYS A LITTLE UNCERTAIN. BUT THIS -- I THINK IT FITS -- THE MANAGEMENT GROUP FELT THAT IT FITTED RELATIVELY WELL. THE GRANTS WORKING GROUP QUESTIONED THAT. SO IT REMAINS QUESTIONABLE, AND I THINK YOU HAVE TO DECIDE YOURSELVES ON IT. I THINK THAT'S REALLY WHERE IT FALLS AT THIS POINT.

DR. JUELSGAARD: TO DISAGREE WITH YOU FOR A MOMENT, I DON'T THINK THAT'S NECESSARILY A DECISION -- I GUESS IT'S A DECISION WE CAN MAKE, BUT I THINK WHAT WE REALLY NEED IS MANAGEMENT'S OPINION ON THAT. AND WHAT I'M HEARING YOU SAY IS THAT IT'S YOUR OPINION THAT IT FITS WITHIN ONE OF THE FOUR GROUPINGS THAT WE'RE ALLOWED TO CONSIDER IN TERMS OF GRANTS. THE GRANTS WORKING GROUP MAY HAVE QUESTIONED THAT, BUT YOUR INITIAL OPINION WAS THIS WAS WORTHY OF REVIEW AS FALLING WITHIN ONE OF THOSE FOUR GROUPS?

DR. TROUNSON: YES. BECAUSE IT WENT THROUGH A PLANNING AWARD, RIGHT. SO WE'VE HAD A COUPLE OF OCCASIONS TO CONSIDER THAT ISSUE. AND I CAN'T REMEMBER THE DISCUSSION AT THE PLANNING

AWARDS. MAYBE SOMEONE ELSE CAN, GIL OR SOMEONE ELSE CAN REMEMBER WHETHER THAT WAS BROUGHT UP AT THAT POINT IN TIME, BUT IT WAS CERTAINLY BROUGHT UP AT THE FINAL DISCUSSION. SO, YES, WE FELT -- I THINK WE'RE FAIR TO SAY THAT MANAGEMENT DIDN'T HAVE STRONG VIEWS ABOUT SAYING THIS WAS OUT OF ORDER AND FELT THAT IF THIS MIGHT BE A MOLECULE THAT ACTUALLY INDUCES ENDOGENOUS CELLS TO ENDOGENOUSLY MULTIPLY IN SOME WAY, THAT FALLS WITHIN OUR PORTFOLIO. SO, GIL, DO YOU RECALL AT ALL?

DR. SAMBRANO: MY RECOLLECTION IS THAT THIS PROJECT IS ONE THAT FELL KIND OF ON THE LINE. THERE WAS QUESTION AS TO WHETHER IT WAS ELIGIBLE OR NOT. AND THE DECISION WAS TO ALLOW THE GRANTS WORKING GROUP ITSELF TO VET THAT, TO CONSIDER THE PROPOSAL. AND SO WE DEEMED IT TO BE ELIGIBLE FOR REVIEW, AND THEN HAVE THE WORKING GROUP DETERMINE THAT.

AT THE PLANNING AWARD STAGE, I THINK IT WAS SUFFICIENT SUCH THAT WE AWARDED THE PLANNING AWARD, BUT THEN THE QUESTION AROSE DURING THE RESEARCH AWARD PROPOSAL AGAIN AS TO WHETHER THIS WOULD QUALIFY. SO, IN ESSENCE, WE LEFT THE QUESTION TO THE GRANTS WORKING GROUP.

DR. TROUNSON: I TAKE IT THAT YOU WOULD

MUCH RATHER US MAKE A FIRM DECISION ON IT. AS IT TURNED OUT IN THIS PARTICULAR CASE, WE WERE SORT OF MAYBE ON THE LINE, MAYBE A LITTLE INSIDE THE LINE, AND THE GRANTS WORKING GROUP WAS OUTSIDE THE LINE IN TERMS OF THEIR PUTTING. SO IT IS A LINE CALL, TO BE HONEST.

DR. FRIEDMAN: JUST A COUPLE OF POINTS, PLEASE. ONE IS THAT ALTHOUGH WE'RE KEENLY INTERESTED IN MECHANISMS AND WHAT'S REALLY HAPPENING HERE, I DON'T WANT TO SEEM TOO FASTIDIOUS IN -- THERE ARE A LOT OF THINGS WE CAN'T PROVE, AND I RECOGNIZE THAT, AND I'M NOT ASKING FOR A LEVEL OF PROOF FOR THIS PROPOSAL THAT WE DON'T HAVE WITH OTHER PROPOSALS.

I THINK THE ANECDOTE THAT WAS DESCRIBED TO US IS A VERY PROVOCATIVE ONE. IT CERTAINLY IS WORTHY OF A LOT OF ATTENTION AND STUDY. AND I'M SURE THAT BOTH IN BOSTON AND IN SACRAMENTO THIS IS BEING LOOKED AT VERY CLOSELY. IT'S A LITTLE HARD, AND I'M NOT AN EXPERT IN THIS AREA, OS AND OTHER PEOPLE ARE, IT'S A LITTLE HARD FOR ME TO UNDERSTAND IF THIS WERE A STEM CELL EFFECT, WHY WE'RE SEEING IT IN A COUPLE OF DAYS. THERE MAY BE VERY GOOD MECHANISMS FOR THAT, AND I'M JUST ADMITTING MY OWN IGNORANCE. I DO SEE THIS AS A POWERFUL, INTERESTING

MOLECULE. I DO SEE THIS AS A REALLY WORTHWHILE THING TO STUDY. AND SO I DON'T CHALLENGE THAT AT ALL, AND WHETHER IT WORKS FOR ALZHEIMER'S OR WHETHER IT MERELY WORKS FOR TRAUMATIC BRAIN INJURY, WOULDN'T THAT BE WONDERFUL? YES, OF COURSE, IT WOULD.

I, AGAIN, AM NOT TRYING TO BE OVERLY FASTIDIOUS, BUT I'M TROUBLED BY A LOT OF QUESTIONS IN THIS REGARD THAT PERHAPS WE'LL HAVE BETTER ANSWERS TO AS SOME OF THE OTHER STUDIES THAT ARE GOING ON COME TO FRUITION.

DR. TROUNSON: WELL, I THINK IT'S NOT GOING TO WORK ON A STEM CELL POPULATION WITHIN A COUPLE OF DAYS. YOU'RE RIGHT. AND EVEN IN A PROGENITOR POPULATION. BUT IT MAY BE A COFACTOR FOR SOMETHING, YOU SEE. AND SO WE'LL ACCEPT THAT IT'S A COFACTOR OF SOME KIND, BUT IT CAN'T -- IT ACTUALLY CAN'T INDUCE A STEM CELL POPULATION IN THAT TIME FRAME.

DR. STEWARD: JUST ACTUALLY A COUPLE OF POINTS AND TO BUILD ON DR. FRIEDMAN'S COMMENTS. WHAT WE'RE SEEING HERE IS A PROPOSAL THAT REPORTS A POSITIVE BENEFIT ON MEMORY AND THAT REPORTS A POSITIVE EFFECT ON STEM CELL PROLIFERATION. AND IN A SENSE WE'RE LOOKING AT THIS AT WHAT WOULD BE NORMALLY A PRETTY EARLY STAGE EXCEPT THAT THIS THING

REALLY CAN GO TO A CLINICAL TRIAL VERY QUICKLY. IF IT WASN'T A DRUG THAT HAD BEEN AROUND FOR A LONG TIME AND TRIED IN OTHER WAYS AND ALREADY IN USE FOR OTHER THINGS, THEN YOU'D WANT TO SEE A LOT OF THIS PROOF OR MAYBE YOU'D WANT TO.

I THINK AT THE END OF THE DAY, REALLY ESTABLISHING DEFINITIVELY ONE WAY ANOTHER WHETHER PROLIFERATION OF STEM CELLS THAT IS INDUCED BY X, Y, OR Z IS ACTUALLY THE CAUSE OF WHATEVER OUTCOME. IT'S GOING TO BE A HUGE ISSUE. LEVELS OF PROOF ARE GOING TO VARY TREMENDOUSLY.

SO WE ARE WHAT WE ARE AT THIS ONE. I THINK WE GAVE IT A PLANNING GRANT. IN A SENSE WE DEFINED IT AS IN SCOPE THEN. TO ME THAT'S SORT OF THE END OF THE STORY ON THAT.

THE SECOND POINT I WANT TO MAKE, THOUGH, IS A LITTLE BIT DIFFERENT, AND IT HASN'T BEEN MADE YET. JUST TO REMIND EVERYBODY THAT ONE OF THE CRITERIA FOR REVIEW OF THESE GRANTS WAS COMMERCIALIZATION POTENTIAL. AND JUST TO SAY, I DO SIT ON THESE REVIEWS AS A PATIENT ADVOCATE. AND THIS WAS AN IMPORTANT CRITICISM OF THIS GRANT BECAUSE IT DOESN'T HAVE IP PROTECTION. SO THE QUESTION WAS RAISED, WELL, HOW ARE YOU GOING TO TAKE IT TO THE NEXT STEP?

AND ALL OF THIS DISCUSSION HAS BEEN ABOUT SCIENCE, AND I THROW THAT OUT THERE. I'M NOT THROWING IT OUT THERE AS A CRITICISM ACTUALLY. I'M THROWING IT OUT THERE BECAUSE THE POINT THAT I MADE IN PROGRAMMATIC CONSIDERATION IS THAT IF THERE'S A BIG POSITIVE EFFECT HERE, BELIEVE ME, WE'LL FIGURE OUT A WAY TO FUND IT. IT JUST DOESN'T, I DON'T THINK, HAVE TO GO THROUGH THE SAME KIND OF PROCESS YOU WOULD CONSIDER FOR ANOTHER DRUG BECAUSE OF THE HUGE NEED. I THINK THAT REALLY WITH PRIVATE FOUNDATIONS AND DONATIONS, I THINK THE FURTHER STEPS IN BRINGING THIS FORWARD COULD ACTUALLY BE ACHIEVED FAIRLY EASILY. SO I JUST WANTED TO MAKE THOSE TWO POINTS. THANK YOU.

CHAIRMAN THOMAS: COMMENTS FROM OTHER MEMBERS OF THE BOARD?

MS. GIBBONS: THANK YOU, MR. CHAIR. I KNOW ALL OF US ARE STRUGGLING WITH TRYING TO FIND SOME COMFORT WITH REGARD TO, AND IT'S A BIG AGENDA ITEM FOR US, WITH REGARD TO WHEN EXTRAORDINARY PETITIONS ARE CONSIDERED AND HOW THINGS ARE BROUGHT FORTH FOR RE-REVIEW AND HOW MUCH TIME PEOPLE HAVE. I DON'T KNOW WHETHER THIS IS AN APPROPRIATE QUESTION OR NOT OR SOMETHING FOR US TO DISCUSS WHEN WE GET TO THAT AGENDA ITEM.

WITH REGARD TO THIS PARTICULAR ONE, I WOULD LIKE TO KNOW WAS THAT NOT MADE CLEAR, OR WHY THE TEAM WAS NOT TIMELY IN COMING FORTH WITH THE MORE STANDARD ROUTE OF EXTRAORDINARY PETITION.

DR. TROUNSON: I KIND OF THINK IT'S SELF-OBVIOUS, LEEZA. THE EXAMPLE SET AT THE LAST BOARD MEETING CERTAINLY INDUCED THE TEAM TO THINK THAT MAYBE THEY SHOULD HAVE DONE IT AS WELL. AND I'M DEAD SURE THAT'S EXACTLY THE REASON. AND SO THERE WERE SUCH A LOT OF THESE THAT WENT THROUGH TO RECONSIDERATION, YOU'RE KIND OF SILLY IF YOU DIDN'T. THAT WAS ESSENTIALLY THE POINT, RIGHT?

MS. GIBBONS: BUT THIS ONE, I THINK, CAME IN AT A DIFFERENT TIME. AM I WRONG?

DR. TROUNSON: YEAH, AFTERWARDS. WHEN IT WAS OBVIOUS THAT IF YOU DID THIS, YOU'D HAVE A CHANCE OF BEING RE-REVIEWED IN SOME WAY.

MS. GIBBONS: SO SHOULD THE ASSUMPTION BE, MAYBE I SHOULD BE ASKING THE TEAM, WAS THERE NOT AN AWARENESS THAT THAT NEEDED TO BE DONE?

DR. TROUNSON: EVERYBODY GOT EXACTLY THE SAME INFORMATION. SO IT WAS CLEAR FROM THE BOARD MEETING THAT WE'D ACTUALLY CHANGED A LITTLE. WE NEVER HAD SUCH A LARGE NUMBER GO THROUGH, AND IT WAS A VERY STRONG INDICATOR, AS YOU'D EXPECT. THE

PEOPLE TAKE NOTICE OF THAT. AND BECAUSE THE STUDIES HADN'T BEEN COMPLETED, YOUR DECISIONS HADN'T BEEN MADE, SO THE TEAM THOUGHT IT WAS REASONABLE TO PUT MORE INFORMATION IN. AND IT WAS CLEARLY -- THAT'S THEIR RIGHT TO DO, BUT IT WASN'T -- BECAUSE IT HAD GONE BEYOND THE EXTRAORDINARY PETITION TIME, WE GAVE IT A LITTLE DIFFERENT NAME, BUT IT'S ESSENTIALLY INFORMATION FOR YOU.

DR. STEWARD: I JUST WANTED TO SAY EXPLICITLY THAT MY COMMENTS AREN'T BASED ON THE EXTRAORDINARY PETITION AT ALL. I THINK THAT THESE COMMENTS WOULD HAVE COME UP IN THE DISCUSSION OF THIS PROJECT BEFORE. IT'S JUST THAT WE TRUNCATED THE CONSIDERATION LAST TIME, YOU MAY REMEMBER, AND THIS ACTUALLY NEVER CAME UP FOR DISCUSSION AT OUR LAST BOARD MEETING. WE DID NOT HAVE -- THERE WAS NEVER A MOTION ON IT. SO THERE WAS NO OPPORTUNITY FOR PUBLIC COMMENT.

CHAIRMAN THOMAS: DR. SAMBRANO.

DR. SAMBRANO: I THINK IT'S IMPORTANT TO KNOW THAT ALL APPLICANTS DO RECEIVE INFORMATION ABOUT THEIR OPTIONS. SO IN TERMS OF SUBMITTING A FORMAL APPEAL, OF SUBMITTING AN EXTRAORDINARY PETITION. NOW, THE PETITION POLICY, HOWEVER, IS, AS YOU KNOW, RATHER VAGUE. AND SO THERE ARE NO REAL

RULES BEHIND WHAT AN EXTRAORDINARY PETITION SHOULD ENTAIL.

SO MY ADVICE TO APPLICANTS IS TO LOOK AT THE POLICY, AND THAT IT'S REALLY UP TO YOU TO DETERMINE WHAT THE CONTENT OF SUCH A PETITION WOULD BE. I THINK THE SPIRIT OF THE PETITION WAS TO BRING FORTH EXTRAORDINARY CIRCUMSTANCES. HOWEVER, I THINK APPLICANTS ALSO HAVE OBSERVED, AND I THINK THE CASE PERHAPS HERE, EXAMPLES IN OTHER PETITIONS THAT ARE SUBMITTED. SO I THINK THAT IS CERTAINLY A REASON WHY NEW PETITIONS MAY COME FORTH.

CHAIRMAN THOMAS: ANY OTHER COMMENTS FROM MEMBERS OF THE BOARD?

MS. GIBBONS: JUST BRIEFLY PROMPTS TO EVERYONE WHO'S BEEN HERE FOR HOURS WAITING TO HAVE YOUR THREE MINUTES, FROM THE SCIENTISTS AND THE INVESTIGATORS AND THE CORPORATE LEADERS AND THE DOCTORS AND, MOST ESPECIALLY, TO THE PATIENT ADVOCATES WHO WERE JUST SO ELOQUENT AND SO COURAGEOUS AND SO WONDERFULLY GENEROUS AT SHARING YOUR STORY, WE ALWAYS APPRECIATE THAT. AND I KNOW YOU GUYS HAVE BEEN HERE A LONG TIME. SO THANK YOU.

(APPLAUSE.)

CHAIRMAN THOMAS: SEEING NO FURTHER COMMENT FROM THE BOARD, I BELIEVE WE CAN, MR.

HARRISON, MOVE TO -- YES.

MR. HARRISON: THERE'S A MOTION ON THE TABLE WITH RESPECT TO THIS APPLICATION. I DON'T BELIEVE ANY PROPRIETARY INFORMATION HAS BEEN IDENTIFIED. SO AT YOUR DISCRETION, CHAIR, WE COULD PROCEED WITH A VOTE ON THIS APPLICATION BEFORE --

CHAIRMAN THOMAS: THE NEXT COMMENT.

DR. PRICE: WHAT IS THIS MOTION?

MR. HARRISON: THE MOTION ON THE FLOOR IS TO APPROVE FUNDING FOR APPLICATION 5410.

CHAIRMAN THOMAS: MARIA, PLEASE CALL THE ROLL.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: NO.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: NO.

MS. BONNEVILLE: JACOB LEVIN.

DR. LEVIN: NO.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: NO.

MS. BONNEVILLE: MICHAEL FRIEDMAN.

DR. FRIEDMAN: NO.

MS. BONNEVILLE: LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG.

STEPHEN JUELSGAARD.

DR. JUELSGAARD: NO.

MS. BONNEVILLE: BERT LUBIN.

DR. LUBIN: NO.

MS. BONNEVILLE: MICHAEL MARLETTA. LEON FINE. PHIL PIZZO. ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.

MS. SAMUELSON: YES.

MS. BONNEVILLE: JONATHAN SHESTACK.

MR. SHESTACK: NO.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: NO.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: NO.

MS. BONNEVILLE: JAMES ECONOMOU.

CHAIRMAN THOMAS: MR. HARRISON.

MR. HARRISON: THE MOTION FAILS.

CHAIRMAN THOMAS: THANK YOU. PUBLIC COMMENT? WE DO VERY MUCH APPRECIATE, AS MS. GIBBONS, POINTS OUT, THANK YOU, EVERYBODY, FOR COMING.

DR. LEWICKI: WELL, THANK YOU. SO I'M JOHN LEWICKI. I'M THE CHIEF SCIENTIFIC OFFICER OF ONCOMED PHARMACEUTICALS, COMPANY DEVELOPING AGENTS FOR CANCER BASED ON PATHWAYS THAT ARE KEY TO CANCER STEM CELLS. AND I WANT TO THANK THE COMMITTEE FOR GIVING ME AN OPPORTUNITY TO SPEAK. WE'RE ACTUALLY AN APPLICATION THAT WAS PRESENTED AT THE LAST MEETING, WENT UNDER RECONSIDERATION, RECEIVED YESTERDAY WORD THAT THE RECOMMENDATION WAS NOT TO FUND, BUT I WANTED TO CLARIFY SOME POINTS THAT WERE RAISED BECAUSE WE THINK THERE WERE SOME REAL MISUNDERSTANDINGS IN THE GRANT.

AND WHAT I WANT TO CONVEY IS THE REAL SCIENTIFIC PASSION ON OUR BEHALF AND OUR CO-PRINCIPAL INVESTIGATOR, DR. LAURA ESSERMAN, OF UCSF, FOR THIS PROJECT BECAUSE WE THINK IT HAS A GREAT PROBABILITY OF BEING SUCCESSFUL.

SO BASICALLY I'LL BE BRIEF HERE, BUT THE PROPOSAL IS REALLY AIMED AT TREATING THE SUBPOPULATION OF BREAST CANCER PATIENTS WHO ARE AT HIGHEST RISK OF RECURRENCE. THESE ARE GENERALLY PATIENTS WITH LARGE HIGH RISK PROFILE TUMORS WHO WERE TREATED IN THE NEOADJUVANT SETTING PRIOR TO SURGICAL RESECTION OF THEIR TUMOR. AND MANY OF THESE PATIENTS FREQUENTLY HAVE RECURRENT DISEASE.

ROUGHLY A THIRD OF THE PATIENTS TREATED IN THIS SETTING HAVE RECURRENT DISEASE AND AS DESCRIBED BY DR. ESSERMAN, WHEN PATIENTS RECUR, MANY OF THEM PROGRESS AND HAVE RECURRENT DISEASE, METASTATIC DISEASE, WITHIN A YEAR, AND ALMOST ALL OF THESE PATIENTS DIE WITHIN THREE YEARS.

SO THAT'S REALLY THE BASIS OF THE APPLICATION. AND THE TARGET WE'RE FOCUSED ON IS THE TARGET CALLED NOTCH, NOTCH 1. NOTCH IS A PATHWAY FUNDAMENTALLY INVOLVED IN STEM CELL BIOLOGY, AND THERE'S BEEN A LOT OF LITERATURE RECENTLY IDENTIFYING NOTCH 1 AS AN ONCOGENIC DRIVER; IN OTHER WORDS, DRIVING TUMORS IN VARIOUS FORMS OF CANCER. AND WE BELIEVE THAT ALSO APPLIES TO BREAST CANCER.

SO WHAT WE DID IS WE DEVELOPED AN ASSAY TO DETERMINE PATIENTS THAT OVEREXPRESS NOTCH 1 WHERE IT MAY BE DRIVING THEIR TUMOR. WE BASICALLY DEVELOPED THIS ASSAY AND APPLIED IT TO THE POPULATION OF PATIENTS WHO HAD RECURRED FOLLOWING NEOADJUVANT TREATMENT. AND WE FOUND THAT ROUGHLY 30 PERCENT OF THESE PATIENTS HAD ELEVATED NOTCH 1 AS OPPOSED TO A ABOUT 10 PERCENT OF THE PATIENTS IN THE GENERAL BREAST CANCER POPULATION. SO WE RATIONALIZE AND HAVE A LOT OF PRECLINICAL DATA THAT SUPPORT OUR HYPOTHESIS THAT NOTCH 1 IS REALLY DRIVING THESE

TUMORS, AND IT'S RESPONSIBLE FOR THE RESISTANCE TO CHEMOTHERAPY IN THESE PATIENTS.

SO WE HAVE AN ANTIBODY TO NOTCH 1. IT'S AT THE IND STAGE. WE EFFECTIVELY FILED OUR IND. WE'D BE POSITIONED TO TREAT PATIENTS QUICKLY, GO INTO A PHASE I A SAFETY STUDY, A PHASE 1 B COMBINATION STUDY WITH CHEMOTHERAPY, AND THEN WE PROPOSE TWO PHASE II STUDIES. SO I'LL BE QUICK HERE.

TWO MISCONCEPTIONS THAT I WANTED TO POINT OUT IN THE GRANT. NO. 1, IT WAS HIGHLIGHTED THAT WE HAVE TO SCREEN 800 PATIENTS TO IDENTIFY PATIENTS THAT WERE CANDIDATES FOR THIS TRIAL, AND THAT WOULD COMPROMISE TIMELINES. WE DON'T HAVE TO SCREEN PATIENTS AT ALL. THE PATIENTS THAT GET ENROLLED ON THIS TRIAL ARE PATIENTS WHO FAIL ON NEOADJUVANT THERAPY. SO BASICALLY THERE'S NO SCREENING REQUIRED WHATSOEVER UNTIL WE'VE IDENTIFIED THOSE PATIENTS, AT WHICH POINT WE WOULD ONLY HAVE TO SCREEN ABOUT 120 TO IDENTIFY 40 PATIENTS THAT WE PROPOSE TO ENROLL IN THE STUDY.

ANOTHER MISCONCEPTION, AND I THINK SOMETHING THAT'S A MISUNDERSTANDING OR SOMETHING THAT'S REALLY HELD AGAINST US IS WE'VE IDENTIFIED THE NOTCH 1 ICD, THE SIGNALING MOLECULE IN THE CELL,

IS A BIOMARKER. AND THE POINT WAS RAISED THAT ALL WE HAVE IS A POLYCLONAL ANTIBODY. WE'RE IN THE PROCESS OF DEVELOPING A MONOCLONAL ANTIBODY, BUT DON'T HAVE IT YET. BUT THAT'S SOMETHING THAT'S VERY DOABLE. OTHERS HAVE MADE SUCH ANTIBODIES. AND IT COULD HAVE BEEN AN EARLY MILESTONE IN THIS PROJECT HAD IT BEEN SUPPORTED FOR FUNDING.

SO JUST ON BEHALF OF BREAST CANCER PATIENTS AND ALL OF US WHO HAVE SPOUSES, FAMILY, FRIENDS WITH BREAST CANCER, I WANT TO REALLY ADVOCATE FOR THIS APPLICATIONS AND HOPE THAT YOU GIVE IT RECONSIDERATION. THANK YOU.

CHAIRMAN THOMAS: THANK YOU. ARE THERE ANY OTHER MEMBERS OF THE PUBLIC WHO HAVE COMMENT? YES, SIR.

MR. HENBERGER: THANK YOU VERY MUCH. MY NAME IS JERRY HENBERGER, AND I'M THE EXECUTIVE DIRECTOR ELECT WITH THE PARKINSON'S ASSOCIATION BASED IN SAN DIEGO. AND YOU ALL HAVE AGREED TO PUT OFF FOR CONSIDERATION DR. LIPTON'S PROPOSAL FOR YOUR NEXT MEETING. I DID PROMISE TWO OF MY BOARD MEMBERS THAT I WOULD READ THEIR COMMENTS TO YOU, AND I'M ACTUALLY EDITING THE ONE FROM THE ATTORNEY BECAUSE YOU GUYS ARE DOING THE REVIEW. AND I APPRECIATE IT SO VERY MUCH, BUT I THINK THERE'S A LOT OF MERITUS

COMMENTS IN HERE. AND THE ATTORNEY, HIS NAME IS MICHAEL THORSNES, AND HE'S A BRILLIANT MAN, AND HE'S BEEN AFFECTED BY PARKINSON'S. HE ACTUALLY GAVE UP HIS PRACTICE TO ADVOCATE FOR PEOPLE WITH PARKINSON'S. I BELIEVE HIS HEART IS SO VERY PURE IN THIS.

SO THESE ARE HIS WORDS. I SPEAK TO YOU AS A FORMER CIVIL TRIAL LAWYER FOR 34 YEARS, A PARKINSON'S PATIENT FOR 12 YEARS, AND THE WINNER OF THE DANIEL T. BRODERICK AWARD FOR INTEGRITY. I WAS ANNUALLY LISTED AS ONE OF THE BEST LAWYERS IN AMERICA, SERVED AS VICE CHAIR OF THE BOARD OF TRUSTEES FOR THE UNIVERSITY OF SAN DIEGO FOR SIX YEARS, AND WAS RECENTLY APPOINTED CHAIRMAN OF THE EXECUTIVE ADVISORY BOARD FOR THE PARKINSON'S ASSOCIATION OF SAN DIEGO.

I, LIKE THOUSANDS OF OTHER PATIENTS, CAN NO LONGER FUNCTION IN MY PROFESSION. I'M NOT SPEAKING TO YOU AS A LAWYER, BUT AS A MEMBER OF THE COMMUNITY THAT YOU'VE AGREED TO PROTECT USING TAX DOLLARS WISELY AND, MORE IMPORTANTLY, FAIRLY IN BOTH PROCEDURE AND SUBSTANCE. THE PURPOSE FOR SPEAKING IS TO ADDRESS THE PROCESSING AND EVALUATION OF THE EXTRAORDINARY REVIEW OF THE APPLICATION GRANT BY STUART LIPTON. THE SYNOPSIS OF THE GRANT WAS

REVIEWED, CIRM MINUTES FROM JULY 24TH MEETING; AND AFTER MEETING WITH DR. LIPTON, DISCUSSED ISSUES WITH THE ICOC POLICY GOVERNING EXTRAORDINARY PETITIONS WITH THE ICOC CONSIDERATION OF APPLICATIONS FOR FUNDING, AND THE BYLAWS OF THE SCIENTIFIC MEDICAL RESEARCH FUNDING WORKING GROUP, AND VARIOUS MEMBERS UNDER THE CIRM WEBSITE.

THIS IS WHERE I'M EDITING. THE URGENCY OF SUBMISSION, REMEDIATION, AND EXCLUSION BE ADDRESSED PROMPTLY AS THIS APPLICATION WAS ONE SUBMITTED BY THE PARKINSON'S DISEASE FOR THE DISEASE TEAM RESEARCH AWARDS, WHICH REQUIRES SPECIFIC ACTIONS WITH FOUR YEARS OF THE DATE FROM THE GRANT. DELAY OF PROCESSING THIS PROJECT WOULD MEAN AS TO ONE MILLION PARKINSON'S PATIENTS IN THE UNITED STATES THAT THE PROMISE OF THIS PROJECT WOULD BE SHELVED.

WE APPRECIATE YOUR CONSIDERATION IN THAT THERE ARE ONE MILLION PARKINSON'S PATIENTS IN THIS COUNTRY. THEIR NEEDS ARE ENTITLED TO A COMPLETE HEARING FREE FROM CONFLICT PARTICIPANTS, AND NOT LIMITED IN PUBLIC RESPONSE SUBJECT TO SELECTIVE EXCLUSION OF EVIDENCE.

AS THE EARLY TEAM DISEASE RESEARCH AWARD APPLICANT DEALING -- AS THE ONLY DISEASE TEAM RESEARCH APPLICATION DEALING WITH PARKINSON'S,

TIMING AND PROPER RESOLUTION OF THE GRANT PROPOSED IS ABSOLUTELY NECESSARY AS IT MUST BE REMEMBERED THAT SPECIFIC MILESTONES OF THE FDA AND RELATED APPROVAL PROCESS MUST BE ACCOMPLISHED WITHIN FOUR YEARS. ANY FURTHER DELAY IN THAT PROCESS WILL AND SHOULD BE REGARDED WITH SADNESS BY THE MILLIONS OF SUFFERERS THAT WAIT IN GREAT FRUSTRATION AS THEY WATCH DELAY IN TESTING STEM CELLS FOR THE TREATMENT OF PARKINSON'S.

ON A MUCH LIGHTER NOTE, THIS IS FROM CHANCELLOR MARY ANNE FOX. AS MANY OF YOU KNOW, I HAVE WORKED WITH COLLEAGUES IN SAN DIEGO TO EXPLORE THE POSSIBILITIES OF ADDRESSING NEUROLOGIC DISEASES LIKE PARKINSON'S THROUGH THE USE OF EITHER ADULT OR EMBRYONIC STEM CELLS. LIKE OTHER DISEASES THAT AFFECT CONTROLLED MOTION, THERE'S NO CURE AND MILLIONS OF PEOPLE AWAITING ENCOURAGEMENT THAT MIGHT PROVIDE RELIEF. IN FACT, I LOOK FORWARD TO A TIME WHEN TALENTED RESEARCHERS MIGHT BE ABLE TO ADDRESS MY OWN CASE, THEREBY ADVOCATING THE GENERAL APPROACH TO PARKINSON'S.

THE GOAL OF PROPOSITION 71 IS, OF COURSE, TO DIRECT FUNDING SCIENTIFIC RESEARCH THAT WILL LEAD TO NEW MEDICAL TREATMENTS AND CURES. TODAY'S CONSIDERATION IS AN OPPORTUNITY TO REVIEW A

TRANSFORMATIONAL RESEARCH PROGRAM THAT COULD DO JUST THAT. I'VE KNOWN STUART LIPTON FOR MANY, MANY YEARS AND RESPECT HIS WORK. I FURTHER APPRECIATE THE PAST PARKINSON'S PROJECTS THAT THE ICOC HAS FUNDED, WHICH HAS LED TO A GREATER UNDERSTANDING OF THE DISEASE. STUART'S PROPOSAL MAY DELIVER ON THE ULTIMATE GOAL OF PROPOSITION 71, WHICH IS TRANSLATIONAL RESEARCH WHICH WILL LEAD TO A CURE IN PARKINSON'S DISEASE IN PATIENTS.

THANK YOU FOR CONSIDERING HER OPINION AND ON THE IMPORTANCE OF THIS GRANT. THANK YOU VERY MUCH.

CHAIRMAN THOMAS: THANK YOU. ANY OTHER COMMENTS BY MEMBERS OF THE PUBLIC?

MR. WONG: MY NAME IS ALBERT WONG. I'M REPRESENTING APPLICATION 5373. I UNDERSTAND THAT YOU'RE PROBABLY GOING TO BRING THIS UP TO FOR VOTE, SO PERHAPS I SHOULD GIVE MY PUBLIC COMMENTS AT THAT TIME.

CHAIRMAN THOMAS: THE PROCEDURE IS WE HAVE ASKED IF THERE WERE ANY MOTIONS TO APPROVE THAT FOR FUNDING. THAT WAS ONE OF THE TWO THAT SUBMITTED ADDITIONAL CORRESPONDENCE.

DR. VUORI: I WOULD LIKE TO HEAR SCIENCE OFFICER'S PRESENTATION ON THIS GRANT.

DR. FEIGAL: I BELIEVE DR. INGRID CARAS IS GOING TO COME UP AND GIVE A SUMMARY OF THAT PROPOSAL.

CHAIRMAN THOMAS: MR. HARRISON, JUST AS A MATTER OF PROCEDURE, DO WE NEED A MOTION TO HAVE THE PRESENTATION?

MR. HARRISON: NO.

DR. CARAS: THIS IS APPLICATION 5373 ENTITLED "RECOMBINANT BISPECIFIC ANTIBODY TARGETING CANCER STEM CELLS FOR THE THERAPY OF GLIOBLASTOMA." SO THE GOAL OF THIS PROJECT IS TO DEVELOP A BISPECIFIC ANTIBODY DESIGNED TO TARGET CANCER STEM CELLS IN GLIOBLASTOMA TUMORS BY SIMULTANEOUSLY BINDING TO TWO RECEPTORS, CD133 AND EGFR VARIANT III COEXPRESSED ON THE SURFACE OF THE GLIOBLASTOMA CANCER STEM CELLS.

THE PROJECT PLAN LAYS OUT TRANSLATIONAL RESEARCH AND DEVELOPMENT ACTIVITIES LEADING TO AN IND FILING.

REVIEWERS DID NOT DISPUTE THAT GLIOBLASTOMA IS A DEVASTATING DISEASE WITH NO EFFECTIVE TREATMENT. HOWEVER, THEY HAD SERIOUS CONCERNS ABOUT THE RATIONALE, READINESS, AND FEASIBILITY OF THIS PROPOSAL.

ON THE RATIONALE, REVIEWERS COMMENTED THAT

IT IS NOT CLEAR THAT THIS PRODUCT WILL BE SUFFICIENTLY SPECIFIC FOR CANCER CELLS AND WILL NOT ALSO TARGET NORMAL CELLS EXPRESSING EITHER RECEPTOR, WHICH RAISES A SIGNIFICANT SAFETY CONCERN. SO FROM A SAFETY PERSPECTIVE, THEY WERE NOT CONVINCED THAT THERE IS AN ADVANTAGE TO HAVING A SINGLE MOLECULE TARGET TWO DISTINCT SURFACE RECEPTORS. AND THEY FELT THAT THE APPLICANT MAY NOT HAVE THOUGHT THROUGH ALL THE POSSIBLE SAFETY CONCERNS.

IN ADDITION, THE RATIONALE IS BASED ON TARGETING OF CELLS THAT COEXPRESS THE TWO RECEPTORS, WHICH MAY REPRESENT A SUBGROUP OF GLIOBLASTOMA STEM CELLS IN A PATIENT THAT DOES NOT TAKE INTO ACCOUNT TUMOR HETEROGENEITY.

REGARDING READINESS, THEY NOTED THAT THE APPLICANT HAS NOT YET SELECTED THE FINAL DEVELOPMENT CANDIDATE, WHICH WAS A PREREQUISITE FOR THIS AWARD. TIMELINES DO NOT APPEAR TO BE FEASIBLE, AND THEY FELT THAT THE PROJECT IS AT A STAGE THAT IS STILL TOO EARLY TO BE TRYING TO FORMALLY DEVELOP THIS PRODUCT FOR IND-ENABLING STUDIES.

THEY NOTED THAT THE PROPOSAL INCLUDES A SIGNIFICANT AMOUNT OF MECHANISTIC AND CELL BIOLOGY WORK WHICH MAY NOT BE NECESSARY FROM A REGULATORY PERSPECTIVE AND THAT MORE EFFORT SHOULD BE FOCUSED

ON DEFINING THE PRODUCT SPECIFICITY, SELECTIVITY, PHARMACOKINETICS, AND SAFETY IN RELEVANT ANIMAL MODELS.

FINALLY, REGARDING FEASIBILITY, A KEY QUESTION CONCERNED WHETHER THE ANTIBODY WILL CROSS THE BLOOD BRAIN BARRIER. GETTING ANTIBODIES ACROSS THE BLOOD BRAIN BARRIER IS A NONTRIVIAL ISSUE. AND SOME REVIEWERS BELIEVE THAT IT'S UNLIKELY THAT THE ANTIBODY WILL EFFECTIVELY CROSS THE BLOOD BRAIN BARRIER BASED ON PREVIOUS STUDIES IN THIS AREA.

A SERIOUS CONCERN IS WHETHER THE CONCENTRATION THAT THEY'LL HAVE TO DELIVER TO A PATIENT TO GET ENOUGH ACROSS THE BLOOD BRAIN BARRIER WILL HAVE TOXIC EFFECTS PERIPHERALLY. IN OTHER WORDS, WILL THEY BE ABLE TO ACHIEVE THERAPEUTIC LEVELS WITHIN THE BRAIN AT SYSTEMIC LEVELS THAT ARE NOT TOXIC. AND REVIEWERS FELT THAT IT WOULD BE IMPORTANT TO CONFIRM THIS BEFORE STARTING IND-ENABLING STUDIES FOR AN INTRAVENOUS ROUTE. SO THOSE WERE THE MAIN CRITICISMS. I'LL BE HAPPY TO ANSWER ANY QUESTIONS.

MR. TORRES: HOW IS THIS DISTINCT FROM OUR CITY OF HOPE PROPOSAL WITH DR. ABOODY?

DR. FEIGAL: I CAN ANSWER THAT QUESTION. THAT'S NEURAL STEM CELLS AS A DELIVERY WITH A

PAYLOAD OF CPT 11. IT'S A VERY DIFFERENT DELIVERY, AND IT'S A PAYLOAD OF A CHEMOTHERAPY AGENT.

CHAIRMAN THOMAS: MR. HARRISON, IS IT APPROPRIATE THAT WE ASK HERE IF SOMEBODY WANTS TO MAKE A MOTION? BECAUSE EITHER WAY WE WILL LET THE PUBLIC COMMENT PROCEED.

MR. HARRISON: YES.

CHAIRMAN THOMAS: OKAY. SO MEMBERS OF THE BOARD, DO WE HAVE A MOTION TO APPROVE FUNDING OF THIS PROPOSAL? HEARING NONE, PROCEED NOW TO PUBLIC COMMENT.

MR. WONG: SO MY NAME IS ALBERT WONG. I'M THE PRINCIPAL INVESTIGATOR ON THE GRANT. I'M A PROFESSOR AT STANFORD UNIVERSITY. I DID HAVE A SERIES OF PREPARED COMMENTS TO ADDRESS MY PROPOSAL. I GUESS I'LL THROW A LOT OF THAT OUT IN LIGHT OF THIS VIEW.

THE FIRST THING I'D LIKE TO POINT OUT IS THAT GLIOBLASTOMA IS A DEVASTATING DISEASE. IT ROBS PEOPLE OF THEIR PERSONALITY AND IMMEDIATELY LEADS TO A DIMINISHED QUALITY OF LIFE. BUT I REMAIN OPTIMISTIC THAT WE CAN CURE THIS DISEASE IN OUR LIFETIME. AND THE REASON THAT I'M SO OPTIMISTIC IS BECAUSE OF THE CANCER STEM CELL THEORY.

CANCER STEM CELLS, AS YOU PROBABLY ARE

AWARE, ARE SORT OF LIKE THE UNDERWORLD OF STEM CELLS. THEY ARE THE ONES THAT GIVE RISE TO THE CANCER, AND THEY ARE THE ONES THAT RESULT IN THE CANCER GROWING. BUT JUST LIKE NORMAL STEM CELLS, IF YOU GET RID OF THOSE CANCER STEM CELLS, YOU PREVENT A TUMOR FROM GROWING. IT'S JUST LIKE KILLING THE ROOT OF A TREE. IF YOU KILL THE ROOTS, YOU STOP THE TREE FROM GROWING.

NOW, THE REASON I'M SO OPTIMISTIC ABOUT OUR TARGET IS THAT PERHAPS IT'S ONE OF THE FIRST CANCER-SPECIFIC CANCER STEM CELL TARGETS AVAILABLE. AND THE REASON I'M SO OPTIMISTIC IS AS A POSTDOCTORAL FELLOW, I HELPED DISCOVER A MOLECULE CALLED EGF RECEPTOR VARIANT III OR EGFRVIII AND. WE DEVELOPED A PEPTIDE VACCINE AGAINST THIS. THIS HAS NOW GONE THROUGH FOUR CLINICAL TRIALS, INCLUDING NOW A MULTINATIONAL PHASE III TRIAL. IT IS THE ONE BIOLOGIC THERAPEUTIC THAT HAS GONE FOR THIS LONG IN GLIOBLASTOMA THERAPY.

A PARADOX, THOUGH, IS ONLY 10 PERCENT OF THE CELLS EXPRESS EGFRVIII. SO HOW CAN A VACCINE BE SO EFFECTIVE WHEN IT'S ONLY ADDRESSING 10 PERCENT OF THE CELLS? WE DID EXPERIMENTS AND SHOWED THAT EGFRVIII IS PRESENT IN THE CANCER STEM CELLS. AND THIS IS WHEN I BECAME REALLY EXCITED BECAUSE EVERY

TIME WE ASKED THE QUESTION ABOUT THESE EGFRVIII POSITIVE CELLS, THEY LOOKED LIKE NORMAL STEM CELLS EXCEPT THEY WERE CANCEROUS.

AND SO THIS PROVIDED AN EXPLANATION FOR WHY THE PEPTIDE VACCINE WAS WORKING, WHY WHEN WE'RE ONLY KILLING 10 PERCENT OF THE CELLS, WE CAN ACTUALLY GET RID OF TUMORS IN PATIENTS. SO WE CAME UP WITH YET ANOTHER THERAPEUTIC BECAUSE VACCINES RELY ON AN ACTIVE IMMUNE SYSTEM. THE PATIENT HAS TO HAVE A GOOD IMMUNE SYSTEM IN ORDER FOR THIS DRUG TO WORK, PLUS PATIENTS HAVE TO WAIT TWO MONTHS PRIOR TO ANY THERAPY IN ORDER TO RECEIVE THE VACCINE.

SO AN ANTIBODY IS A PASSIVE IMMUNE THERAPY. YOU CAN GIVE IT TO A PATIENT IMMEDIATELY. AND SO WE ALSO WANTED TO SPECIFICALLY ADDRESS THE CANCER STEM CELL POPULATION. AND SO WE DEVISED A MOLECULE THAT NOT ONLY RECOGNIZES THE EGFRVIII POSITIVE CELLS, BUT ALSO PROVIDES FURTHER SPECIFICITY USING THE MOLECULE CD133, WHICH IS PRESENT ON NORMAL NEURAL STEM CELLS.

DOING THAT, AND THIS IS WHERE I NEED TO -- THE REASON OUR MOLECULE, I THINK, IS UNIQUE AND WAS OVERLOOKED BY THIS COMMITTEE IS WE ARE NOW SIGNIFICANTLY REDUCING THE AMOUNT OF ANTIBODY NECESSARY IN ORDER TO TREAT A PATIENT. AND LET ME

JUST SAY THAT ALL OF THE SCIENTIFIC COMMENTS PRESENTED HAVE BEEN ADDRESSED IN THE LETTER THAT I SENT TO THE COMMITTEE AS WELL AS A REBUTTAL LETTER THAT I SENT TO THE CIRM STAFF.

PART OF THE REASON THAT I'M HERE TODAY SO LATE IN THE PROCESS IS THAT WE WERE PURSUING ANOTHER APPEAL PROCESS WITH CIRM VIA THE CONFLICT OF INTEREST POLICY, BUT IT APPEARS REALLY THAT WE SHOULD HAVE APPEALED TO CIRM BASED ON THIS EXTRAORDINARY PETITION SEVERAL MONTHS AGO.

LET ME ALSO FINALLY MENTION THAT THIS IS NOT THE FIRST TIME CIRM HAS EXAMINED THIS PARTICULAR MOLECULE. WE ACTUALLY SUBMITTED THIS AS AN ET III APPLICATION IN THIS MOST RECENT ROUND. IT ACTUALLY SCORED EXTREMELY WELL THERE. THE APPLICATION JUST ABOVE OURS AND SEVERAL BELOW OURS WERE ACTUALLY SELECTED FOR FUNDING. SO WE FEEL THAT THERE WAS CONSIDERABLE MERIT TO OUR APPROACH THAT WAS OVERLOOKED IN THIS PARTICULAR REVIEW. AND REALLY MY APPEARANCE HERE TODAY IS TO POINT OUT THE DEFICIENCIES IN THAT REVIEW. I'M NOT GOING TO GET INTO IT BECAUSE I'M PRESSED FOR TIME. BUT ALSO, IT'S WELL DOCUMENTED IN OUR LETTER TO CIRM BEFORE THE PANEL AS WELL AS IN ANOTHER LETTER TO CIRM.

SO CLEARLY I'M DISAPPOINTED IN THE REVIEW,

BUT THERE'S CERTAINLY A LOT OF DATA OUT THERE THAT WILL REFUTE THE NEGATIVE REVIEW THAT WE RECEIVED FROM THE GWG. THANK YOU FOR YOUR TIME.

CHAIRMAN THOMAS: THANK YOU, DOCTOR. ARE THERE ANY PROJECTS IN TIER III THAT ANY MEMBER OF THE BOARD WOULD LIKE TO MOVE UP TO TIER I FOR FUNDING? HEARING NONE, MR. HARRISON, COULD YOU WALK US THROUGH -- I GUESS WE WILL NOW GO INTO CLOSED SESSION; IS THAT CORRECT?

MS. SAMUELSON: MR. CHAIRMAN, I'D LIKE TO JUST ASK WHEN IS THE APPROPRIATE TIME TO DO WHATEVER IS NECESSARY TO PROTECT THE PARKINSON'S DISEASE TEAM GRANT SO THAT IT DOESN'T FALL INTO SOME PROCEDURAL HOLE?

CHAIRMAN THOMAS: I HAVE PULLED IT OUT OF TIER III AND TABLED IT FOR THE NEXT MEETING.

MS. SAMUELSON: THANK YOU VERY MUCH.

CHAIRMAN THOMAS: MR. HARRISON.

MR. HARRISON: THE BOARD WILL NOW CONVENE IN CLOSED SESSION TO CONSIDER PROPRIETARY INFORMATION RELATING TO THE DISEASE TEAM THERAPY DEVELOPMENT AWARD APPLICATIONS PURSUANT TO HEALTH AND SAFETY CODE SECTION 125290.30(F)(3)(B) AND (C).

CHAIRMAN THOMAS: LOGISTICALLY IS THAT BACK IN THE ROOM TO THE RIGHT WHERE WE GOT THE

DINNER? THANK YOU.

MR. SHEEHY: JUST COULD WE FIND OUT WHICH APPLICATIONS WE'RE CONSIDERING?

CHAIRMAN THOMAS: HOLD ON PLEASE. HOLD ON. MR. HARRISON, WOULD YOU LIKE TO.

MR. SHEEHY: MAYBE WE SHOULD CLARIFY THAT.

MR. HARRISON: THE BOARD WILL JUST BE CONSIDERING PROPRIETARY INFORMATION WITH RESPECT TO ONE APPLICATION, AND THAT'S APPLICATION 5416.

MR. SHEEHY: GREAT. SO THOSE IN CONFLICT SHOULD NOT GO ACROSS THE HALL.

MR. HARRISON: CORRECT.

(THE BOARD THEN WENT INTO CLOSED SESSION, NOT REPORTED NOR HEREIN TRANSCRIBED. THE FOLLOWING WAS THEN HEARD IN OPEN SESSION:)

CHAIRMAN THOMAS: IF EVERYBODY COULD PLEASE TAKE THEIR SEATS.

MR. HARRISON: WE HAVE A MOTION THAT IS ON THE TABLE TO APPROVE FUNDING FOR APPLICATION 5416. THE MEMBERS WHO ARE RETURNING ARE IN CONFLICT WITH RESPECT TO THAT APPLICATION. SO PERHAPS WE CAN BEGIN.

CHAIRMAN THOMAS: OKAY. SO WE'VE HAD OUR CLOSED SESSION. LET'S REOPEN THIS TOPIC FOR DISCUSSION. WHO WOULD LIKE TO START?

MR. TORRES: I WOULD LIKE THE CHAIR TO START WITH HIS PROPOSAL.

DR. PRICE: IS THERE A MOTION ON THE TABLE?

CHAIRMAN THOMAS: THERE IS A MOTION ON THE TABLE AND IT HAS BEEN DISCUSSED. THERE HAVE BEEN CONCERNS EXPRESSED ABOUT THE FACT THAT THIS WOULD BE THE SECOND AWARD GOING TO THE SAME COMPANY, THAT IT REQUIRES MATCHING FUNDING THAT THEY'VE SAID THEY WILL PUT UP. BUT BECAUSE CIRM WOULD ACCOUNT FOR SUCH A LARGE PART OF THE ASSETS OF THIS COMPANY, WITH RESPECT TO THIS PARTICULAR AWARD, WE FEEL THAT WE WOULD LIKE, AT LEAST I WOULD LIKE TO PROPOSE THAT WE ENTERTAIN A REQUIREMENT THAT THE COMPANY SHOW THE MATCHING FUNDS IN ORDER TO GET ACCESS TO FUNDING THAT WE WOULD GIVE THEM VIA THIS AWARD.

MR. TORRES: I SECOND THAT MOTION.

CHAIRMAN THOMAS: IT'S NOT REALLY A MOTION. THAT'S ME DESCRIBING IT.

MR. TORRES: I MOVE YOUR AMENDMENT TO THE MAIN MOTION.

CHAIRMAN THOMAS: SO MR. HARRISON IS WAVING FRANTICALLY.

MR. HARRISON: SO THERE IS A MOTION ON THE TABLE. SO IF YOU WOULD LIKE TO OFFER A FRIENDLY

AMENDMENT TO THE --

MS. GIBBONS: I ACCEPT.

CHAIRMAN THOMAS: AND, MR. SENATOR, I BELIEVE YOU WERE THE SECOND ORIGINALLY WAY BACK WHEN. DO YOU ACCEPT THE FRIENDLY AS WELL?

MR. TORRES: I'M VERY FRIENDLY WITH LEEZA ON THIS ISSUE, AND WE SUPPORT EACH OTHER ON THIS ISSUE.

CHAIRMAN THOMAS: OKAY. SO FURTHER DISCUSSION? THERE WERE A NUMBER OF ISSUES BROUGHT UP IN EARLIER DISCUSSION. WOULD LIKE TO GET MEMBERS' VIEW ON ANYTHING THEY'D LIKE TO DISCUSS. MR. SHESTACK, YOU LOOK LIKE YOU'RE ABOUT TO COMMENT.

MR. SHESTACK: I WAS JUST TRYING TO UNDERSTAND WHAT MAYBE STAFF'S POINT OF VIEW WAS PHILOSOPHICALLY ABOUT THE FACT THAT THIS IS ESSENTIALLY THE SAME CELL LINE THAT WE WOULD BE PUTTING $40 MILLION INTO. SO IF WE FUNDED THIS, WE WOULD BE PUTTING ABOUT THAT MUCH INTO IT. WE'RE ALREADY -- SO I DON'T KNOW. IT JUST SEEMS LIKE I WISH SOMEBODY WOULD EXPLAIN HOW IS THAT TYPICAL, A HUNDRED PERCENT KOSHER, A LITTLE BIT OF A GRAB. EXPLAIN IT TO ME BECAUSE I JUST DON'T UNDERSTAND IT.

DR. FEIGAL: WE EVALUATE PROPOSALS BASED ON THE SCIENCE OF EACH INDIVIDUAL PROPOSAL. I THINK

YOU'VE HEARD WHAT SOME OF THE OTHER PROPRIETARY ISSUES MIGHT BE REGARDING THIS. YOU'VE HEARD THE CONCERNS. YOU'VE ALREADY HEARD THE SCIENTIFIC ISSUES THAT WERE ALREADY RAISED BY THE SCIENTIFIC STAFF IN TERMS OF THE EXTENT OF EVIDENCE TO GO INTO THIS DISEASE.

SO I DON'T THINK I NEED TO REITERATE THAT AGAIN. I THINK YOU'VE HEARD THE POINT OF VIEW OF THE SCIENTIFIC STAFF AND FROM THE GRANT REVIEW GROUP.

CHAIRMAN THOMAS: OKAY. I'M NOT SURE THAT ANSWERED HIS QUESTION.

DR. FEIGAL: RIGHT NOW WE DON'T -- RIGHT NOW IN FUTURE INITIATIVES, WE'RE NOT GOING TO ALLOW COMPANIES TO APPLY FOR MORE THAN ONE PROJECT IN THE SAME INITIATIVE. JUST BECAUSE WE KNOW THE DEMAND IS GREAT, AND WE WANT THEM TO PUT THEIR BEST FOOT FORWARD. AT LEAST THAT'S WHAT WE'RE GOING TO PROPOSE TAKE PLACE FOR FUTURE INITIATIVES.

CHAIRMAN THOMAS: WITH RESPECT TO MR. SHESTACK'S QUESTION SPECIFICALLY, THERE'S NOTHING SCIENTIFICALLY THAT PRECLUDES THE USE OF THE SAME CELL LINE FOR TWO DIFFERENT APPLICATIONS.

DR. FEIGAL: NO. IF THAT WAS YOUR QUESTION, NO. IF THERE IS EVIDENCE TO SUPPORT USING

THAT CELL LINE IN THE DISEASE, THAT'S WHAT WE'RE LOOKING AT. IN AND OF ITSELF, USING THE SAME CELL LINE FOR OTHER INDICATIONS IS NOT SOMETHING UNUSUAL. SO IT'S REALLY THE EVIDENCE TO SUPPORT IT.

MS. GIBBONS: JUST A COMMENT ABOUT SOMETHING DR. FEIGAL JUST SAID REGARDING LIMITING COMPANIES AND ROUNDS OF THEIR ABILITY TO WRITE APPLICATIONS FOR PARTICULAR PROPOSALS. BUT WE HAD TALKED EARLIER ABOUT -- I THINK YOU HAD TALKED ABOUT ECONOMIC EFFICIENCY. AND WOULD THERE NOT BE SOME ARGUMENT THAT HAVING MULTIPLE APPLICATIONS IN THE SAME REALM WITH THE SAME LINE, WOULD THAT NOT ALLOW FOR AND OFFER ECONOMIC POTENTIAL, ECONOMIC EFFICIENCY?

DR. FEIGAL: LET ME REPHRASE IT. WE WOULD LOOK FOR REDUNDANCY IN MANUFACTURING OF THE CELL LINE AND SOME OF THE STUDIES. SO THERE MAY BE COSTS THAT AS A STANDALONE THEY'VE ASKED FOR, BUT PERHAPS THERE'S REDUNDANCIES THAT WE WOULD BE LOOKING FOR.

CHAIRMAN THOMAS: WE HAVE A COMMENT WHICH I ASSUME IS DIRECTLY AIMED AT A QUESTION OR TOPIC UNDER DISCUSSION. SIR, PLEASE PROCEED.

MR. MC GLYNN: THANK YOU. MARTIN MCGLYNN, PRESIDENT AND CEO OF STEM CELLS, INC. I JUST WANT TO CLARIFY A COUPLE OF THINGS. FIRST OF ALL, WE

WILL NOT BE USING THE SAME CELL LINES FOR THIS FIELD OF ENDEAVOR. WE WILL BE USING THE SAME PHENOTYPE. BUT WE HAVE MULTIPLE CELL LINES, MULTIPLE CELL BANKS THAT ARE DEDICATED TO DIFFERENT PROGRAMS AND DIFFERENT PROJECTS. SO I JUST WANTED TO MAKE THAT CLEAR.

SECONDLY, WITH REGARD TO ECONOMIES OF SCALE, YES, WE HAVE RECEIVED A DISEASE TEAM AWARD TO SUPPORT OUR CERVICAL SPINAL CORD INJURY PROGRAM, AND WE HAVE APPLIED FOR DISEASE TEAM FUNDING FOR THIS ALZHEIMER'S PROJECT ON THE BASIS THAT THESE ARE TWO STANDALONE PROJECTS.

IN THE EVENT THAT THE COMPANY FINDS ITSELF THE RECIPIENT OF AN AWARD TO FUND THE ALZHEIMER'S PROGRAM, THERE WOULD BE ECONOMIES OF SCALE THAT WOULD COME INTO PLAY IN THE CONDUCT OF BOTH IN TERMS OF CORPORATE RESOURCES, CORPORATE OVERHEAD, AND MANUFACTURING QUALITY CONTROL, ETC. AND THOSE ECONOMIES OF SCALE, I WOULD PRESUME, WOULD BE ADDRESSED IN THE NEXT STEP OF INTERACTIONS WITH CIRM STAFF WHERE THE BUDGETS WOULD BE REVIEWED IN GREAT DETAIL BEFORE ANY FUNDING WENT OUT THE DOOR.

CHAIRMAN THOMAS: THANK YOU. ADDITIONAL COMMENTS?

DR. POMEROY: SO THIS IS A QUESTION, I

THINK, FOR DR. FEIGAL. THIS PROCESS WAS REALLY ABOUT REVIEWING NEW INFORMATION. SO I JUST WANT TO UNDERSTAND WHAT THE NEW INFORMATION REALLY IS BECAUSE THE PETITION TALKED ABOUT A MANUSCRIPT WHICH WE NOW UNDERSTAND WILL REQUIRE MAJOR REVISIONS BEFORE IT WOULD BE CONSIDERED FOR ACCEPTANCE.

SO BEYOND THAT, IS THERE NEW INFORMATION FOR US TO CONSIDER?

DR. FEIGAL: NO. THE NEW INFORMATION WAS SUPPOSED TO BE ABOUT MIGRATION OF THE HUMAN CELLS THAT WERE BEING GIVEN FOR DELIVERY IN ALZHEIMER'S DISEASE. THE MANUSCRIPT WAS REFERRED TO AT THE JULY ICOC WAS THE ONE I DESCRIBED, WHICH IS A DIFFERENT -- THEY WERE MOUSE CELLS, AND IT WAS A DIFFERENT ISSUE.

IN ADDITION, THEY SUBMITTED OTHER CONFIDENTIAL INFORMATION WHICH WE ALLUDED TO IN TERMS OF OTHER DISEASE STATES IN DIFFERENT ANATOMIC SITES OF DELIVERY.

DR. POMEROY: THANK YOU.

CHAIRMAN THOMAS: DEAN PULIAFITO.

DR. PULIAFITO: SOUNDS LIKE AN INTERESTING PROJECT, BUT THE INITIAL REVIEW SHOWED GREAT VARIATION. SOME PEOPLE LOVED IT, SOME PEOPLE DIDN'T LIKE IT. WE ASKED FOR RE-REVIEW AND THE RE-REVIEW

WAS NOT TO FUND. SO...

CHAIRMAN THOMAS: ADDITIONAL COMMENTS? I WOULD JUST LIKE TO GO BACK TO ONE THING WITH RESPECT TO THE SCIENCE HERE, WHICH IS THERE'S DEBATE ABOUT WHETHER THERE'S MIGRATION OR NOT. IF YOU LISTENED TO THE REVIEW, YOU WOULD HAVE HAD SOME DIFFERENCES OF OPINION ON THAT TOPIC. VERY DIFFICULT FOR US TO SIT HERE AND EVALUATE. HOWEVER, HAVING SAID THAT, WITH RESPECT TO PRECLINICAL RESULTS FROM LOCALIZED INJECTION INTO THE HIPPOCAMPUS SPECIFICALLY DEMONSTRATING REAL PRECLINICAL RESULTS WITH RESPECT TO RESTORATION OF MEMORY, I NEVER HEARD THAT REFUTED. AND TO THE EXTENT, YES, IT'S IN MICE, NO QUESTION ABOUT IT. WOULD IT TRANSLATE INTO HUMANS? WE DON'T KNOW. BUT THAT'S SORT OF WHAT THE NEXT STEP, TO ME, WOULD LOGICALLY BE WITH RESPECT TO THAT POSITIVE DATA FOR THAT PARTICULAR PROCEDURE.

SO TO ME IF THAT WERE TO PAN OUT, THAT WOULD BE HUGE. AND I THINK THAT THAT'S SOMETHING THAT WE OUGHT TO TAKE INTO CONSIDERATION.

OTHER COMMENTS? CALL FOR THE QUESTION. MARIA, PLEASE CALL THE ROLL. REPEAT THE MOTION.

MR. HARRISON: AS I UNDERSTAND IT, THE MOTION IS TO APPROVE FUNDING FOR APPLICATION 5416 SUBJECT TO THE REQUIREMENT THAT THE COMPANY

DEMONSTRATE THAT IT HAS ACCESS TO THE MATCHING FUNDS NECESSARY TO COMPLETE THE PROJECT.

CHAIRMAN THOMAS: CORRECT. UNTIL SUCH TIME AS THEY DEMONSTRATE THAT, THEN THEY DO NOT HAVE ACCESS TO THE FUNDING. MARIA, PLEASE CALL THE ROLL.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: NO.

MS. BONNEVILLE: MICHAEL FRIEDMAN.

DR. FRIEDMAN: NO.

MS. BONNEVILLE: LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: BERT LUBIN.

DR. LUBIN: NO.

MS. BONNEVILLE: CLAIRE POMEROY.

DR. POMEROY: NO.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: CARMEN PULIAFITO.

DR. PULIAFITO: NO.

MS. BONNEVILLE: JOAN SAMUELSON.

MS. SAMUELSON: YES.

MS. BONNEVILLE: JONATHAN SHESTACK.

MR. SHESTACK: ABSTAIN.

MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: KRISTINA VUORI.
DR. VUORI: YES.
MR. HARRISON: THE MOTION CARRIES SEVEN TO FIVE.
CHAIRMAN THOMAS: THANK YOU, MR. HARRISON.
MEMBERS OF THE BOARD, I BELIEVE THAT -- OH, NO, THE TIER III. SO LET'S NOT FORGET THEM. MR. HARRISON, WHAT IS THE APPROPRIATE NEXT MOTION HERE?
MR. HARRISON: THE NEXT STEP WOULD BE FOR A DISINTERESTED MEMBER, THAT IS, A MEMBER WHO DOES NOT HAVE A CONFLICT WITH RESPECT TO ANY OF THE APPLICATIONS THAT REMAIN IN TIER III, TO MAKE A MOTION TO CLOSE FUNDING FOR TIER III.
MR. TORRES: SO MOVED.
MR. JUELSGAARD: SECOND THAT MOTION.
CHAIRMAN THOMAS: MR. JUELSGAARD. IT'S BEEN MOVED AND SECONDED. ANY DISCUSSION? PUBLIC COMMENT? HEARING NONE, MARIA, CALL THE ROLL.
MR. HARRISON: JUST A REMINDER FOR MEMBERS WHO DO HAVE A CONFLICT WITH RESPECT TO APPLICATIONS

IN TIER III, PLEASE VOTE YES OR NO EXCEPT WITH RESPECT TO THOSE APPLICATIONS FOR WHICH YOU HAVE A CONFLICT.

YOU SHOULD ALL HAVE A SHEET IN FRONT OF YOU THAT IDENTIFIES THE APPLICATIONS IN WHICH YOU HAVE A CONFLICT.

MS. BONNEVILLE: ROBERT PRICE.

DR. PRICE: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: JACOB LEVIN.

DR. LEVIN: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: MARCY FEIT. MICHAEL FRIEDMAN.

DR. FRIEDMAN: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG. SAM

HAWGOOD.

DR. HAWGOOD: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: SHERRY LANSING. BERT LUBIN.

DR. LUBIN: YES.

MS. BONNEVILLE: MICHAEL MARLETTA. LEON FINE. PHIL PIZZO. CLAIRE POMEROY.

CLAIRE POMEROY.

DR. POMEROY: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: CARMEN PULIAFITO.

DR. PULIAFITO: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: ROBERT QUINT. DUANE ROTH. JOAN SAMUELSON.

MS. SAMUELSON: YES.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: JONATHAN SHESTACK.
MR. SHESTACK: YES.
MS. BONNEVILLE: OSWALD STEWARD.
DR. STEWARD: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: KRISTINA VUORI.
DR. VUORI: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.
MS. BONNEVILLE: JAMES ECONOMOU.
CHAIRMAN THOMAS: MR. HARRISON, NOW DO WE NEED SOME SORT OF OMNIBUS WRAP-UP WE APPROVE OF EVERYTHING, OR IS THAT IT?
MR. HARRISON: WE ARE OFFICIALLY DONE WITH THE DISEASE TEAM THERAPY DEVELOPMENT AWARD APPLICATIONS.
(APPLAUSE.)
DR. POMEROY: CAN I JUST ASK HOW MUCH MONEY WE ENDED UP ALLOCATING IN THE END FOR THE DISEASE TEAM GRANTS?
MS. SAMUELSON: WE AREN'T QUITE DONE. WE HAVE ONE MORE NEXT TIME.

DR. POMEROY: TO THIS POINT, AND DR. BRENNER KNOWS THE ANSWER TO THIS, SO WHAT IS IT?

DR. SAMBRANO: IT'S 214 MILLION.

DR. POMEROY: 214.

MS. SAMUELSON: AND THE BUDGETED AMOUNT WAS 240. AND IT SEEMED IT WAS LOWER PROPORTIONATELY IN SOME REGARD OR OTHER. I CAN'T DOCUMENT IT NOW, SO I'LL JUST STOP. FOR SUCH AN IMPORTANT CATEGORY IN OUR PORTFOLIO, IF THERE'S ANY QUESTION OF SLOWING DOWN THE BASE OF THESE GRANTS GETTING INTO THE PIPELINE AND MOVING FAST, I THINK WE SHOULD MAKE SURE WE HAVE ENOUGH MONEY TO DO IT, WE REALLOCATE WHERE WE NEED TO.

CHAIRMAN THOMAS: OKAY. MEMBERS OF THE BOARD, IF YOU WOULD JUST BEAR WITH ME A FEW MORE MINUTES, I'M VERY CONCERNED THAT IF WE PUT TOO MUCH OVER TO TOMORROW, WE'RE GOING TO END UP LOSING QUORUM AND RUNNING INTO ALL SORTS OF PROBLEMS. SO SINCE WE'RE ALL HERE AT THE MOMENT, I'D LIKE TO PUSH THROUGH A FEW MORE ITEMS.

FIRST OF ALL, DO I HEAR ON ITEM 12, AN ITEM THAT SHOULD BE REQUIRE LESS THAN NO DISCUSSION, DO I HAVE A MOTION TO APPROVE THE MINUTES?

MR. TORRES: SO MOVED.

MS. SAMUELSON: SECOND.

CHAIRMAN THOMAS: MOTIONS RIGHT AND LEFT. ALL THOSE IN FAVOR PLEASE SAY AYE. OPPOSED? ABSTENTIONS?

MARCY, YOU STILL ON THE PHONE?

I'D LIKE TO PROCEED TO ITEM 15, THE CONSIDERATION OF THE PROPOSED AMENDMENT TO THE IP REGS.

MS. BONNEVILLE: J.T., CAN WE JUST FIND OUT WHO WAS THE FIRST AND SECOND ON THAT MOTION?

CHAIRMAN THOMAS: EVERYBODY IN THE ROOM INCLUDING THE AUDIENCE. WHO MOVED?

MR. SHEEHY: I DID.

MS. SAMUELSON: I SECONDED.

CHAIRMAN THOMAS: SO ITEM 15, APPROVAL OF THE IP REGS. ELONA.

MS. BAUM: GREAT. THANK YOU VERY MUCH FOR CONSIDERING THIS MATTER. THIS IS AN ITEM THAT ACTUALLY APPEARED ON THE AGENDA LAST MONTH, AND WE DIDN'T HAVE TIME TO ADDRESS IT. SO I APPRECIATE THE EXTRA EFFORT TO DO SO NOW. I THINK IT'S VERY IMPORTANT IN A NUMBER OF RESPECTS, IN PARTICULAR TO SUPPORT THE STRATEGIC PARTNERSHIP FUNDING PROGRAM AND TO ENGAGE INDUSTRY. THAT WAS A LOT OF THE GENESIS THAT'S INVOLVED HERE.

I'LL GO AS QUICK AS YOU'LL LET ME, KNOWING

THAT IT'S BEEN FULLY BRIEFED IN YOUR BINDERS. AND IF YOU HAVE ANY QUESTIONS, FEEL FREE TO ASK ME ALONG THE WAY.

ESSENTIALLY THERE'S FOUR OBJECTIVES WHEN WE WERE ARRIVING AT THESE PROPOSED AMENDMENTS. AND WHAT WE WERE SEEKING TO DO IS, ONE, SMOOTH OUT THE PAYMENT STREAM. AS YOU CAN SEE, THAT WOULD OBVIOUSLY BE SOMETHING THAT INDUSTRY WOULD BE INTERESTED IN.

TWO, ALSO WANTED TO EXTEND THE REVENUE SHARING OBLIGATION SO THAT THEY ACTUALLY APPLY TO THE COMMERCIALIZING ENTITY WITH RESPECT TO REVENUE SHARING THAT WE OBTAIN FROM COMMERCIAL SALES. WITH RESPECT TO THE LICENSING REVENUE THAT WE SHARE, FOR INSTANCE, ARISING FROM LICENSES, MOST LIKELY FROM NON-PROFITS, WE WANTED TO ADD A LITTLE MORE CLARIFICATION TO THE PROPORTIONALITY CALCULATION THAT PERTAINS TO THE ROYALTY RATE IN THAT SENSE. BUT WE WANTED TO KEEP IN MIND THAT SINCE WE HAD OBTAINED SO MUCH INPUT FROM THE NON-PROFITS, THAT WE WANTED TO MAINTAIN TO THE HIGHEST DEGREE POSSIBLE THE SAME IMPACT ON THEM. IN OTHER WORDS, NOT IMPACT OR CHANGE THE REGULATIONS AS IT APPLIED TO THEM EXCEPT WITH RESPECT TO THE PROPORTIONALITY CLARIFICATION THAT WE WERE OFFERING.

ONE POINT I WANT TO EMPHASIZE BECAUSE I THINK IT REALLY DOES BEAR EMPHASIS IS THAT WE'RE NOT CHANGING ANYTHING THAT WOULD MEAN THAT THE REVENUES THAT WE SHARE GO TO CIRM VERSUS THE STATE OF CALIFORNIA. THEY WILL CONTINUE TO ALWAYS GO TO THE STATE OF CALIFORNIA. WE THINK THAT THIS NEW PARADIGM WE'RE APPLYING WILL BE EASIER TO IMPLEMENT AND HAVE A COMPARABLE IMPACT FINANCIALLY TO THE STATE. SO I THINK THAT BEARS MENTIONING.

SO LET ME JUST WALK THROUGH FIVE KEY CONCEPTS WHICH I THINK CAPTURE ALL OF THOSE TRACK CHANGES THAT YOU SEE. AND BEFORE DOING SO, LET ME REMIND YOU THAT THAT IS A MATTER THAT HAS BEEN CONSIDERED AT DEPTH BY THE IP AND INDUSTRY SUBCOMMITTEE IN JUNE OF THIS YEAR. SO THIS HAS BEEN VETTED VERY THOROUGHLY. AND BY A UNANIMOUS VOTE OF ALL THOSE PRESENT, THE SUBCOMMITTEE RECOMMENDED THAT THESE SETS OF AMENDMENTS BE APPROVED BY THE BOARD TODAY. AND UPON SUCH APPROVAL, IT WOULD SIMPLY START A REGULATORY RULEMAKING PROCESS. SO THERE WOULD BE OPPORTUNITY FOR THE PUBLIC TO COMMENT AGAIN; AND IF ANY ADDITIONAL MATTERS CAME TO OUR ATTENTION THAT WE THOUGHT SHOULD GO TO THE BOARD'S ATTENTION, WE WOULD CERTAINLY BRING THEM TO YOU WITH SOME ADDITIONAL PROPOSED AMENDMENTS.

SO I'LL GO THROUGH THE SET OF FIVE KEY CHANGES. FIRST ONE RELATES TO SECTION 100608 A. AND IT, AGAIN, RELATES TO THE LICENSING REVENUE ASPECTS OF OUR REVENUE SHARING PROGRAM. AS I INDICATED, THERE IS THIS REDUCTION OF THE 25-PERCENT ROYALTY RATES BY A FRACTION OF THE AMOUNT OF FUNDING THAT CIRM FUNDS COMPARED TO THE COST OF THE FUNDING TO DEVELOP THE CIRM-FUNDED INVENTIONS AND TECHNOLOGY. UNDER THE CURRENT APPROACH, IT'S A LITTLE VAGUE AS TO HOW TO CALCULATE THAT BECAUSE WE DON'T SAY OVER WHAT TIME PERIOD.

MY UNDERSTANDING WAS AND IS THAT THE TIME PERIOD WAS ALWAYS INTENDED TO BE THE TIME PERIOD DURING WHICH THE CIRM-FUNDED PROJECT EXISTED. SO WE CLARIFIED THAT, AND IT'S BEFORE YOU IN NOT ONLY THE DOCUMENTATIONS IN YOUR BINDER, BUT UP HERE ON THE SCREEN.

NOW WHAT WE'RE SAYING IS THAT -- WHAT WE'RE SAYING NOW, AND I'LL EXPLAIN A LITTLE BIT OF THE CHANGE IN A SECOND, IS THAT IF CIRM FUNDS 50 PERCENT OR MORE OF THE CIRM-FUNDED PROJECT DURING THE PROJECT PERIOD, THAT'S THE CLARIFICATION OF THE TIMELINE, WHICH GIVES RISE TO THE CIRM-FUNDED INVENTION OR TECHNOLOGY, THEN THE ROYALTY SHARE IS 25 PERCENT. IF WE FUND LESS THAN 50 PERCENT, IT'S

15 PERCENT RATHER THAN SORT OF DOING THIS SPECIFIC CALCULATION AS TO THE PRECISE AMOUNT OF FUNDING. AND WE CLARIFIED AGAIN THAT IT WAS DURING THE PROJECT PERIOD. SO THAT'S THE FIRST CHANGE. I HOPE THAT'S MAKING SENSE AT THIS LATE HOUR, AND I HOPE I'M BEING CLEAR ENOUGH ON THAT.

DR. POMEROY: CAN I ASK A QUESTION ABOUT THAT? SO IF THEY PUT, LIKE, YOU KNOW, 50 MILLION IN UP TO THE POINT TO GET IT READY FOR THE CIRM PROJECT, THEN NONE OF THAT COUNTS IN THE CALCULATION OF WHAT THEY PUT IN BECAUSE IT'S ONLY THE PROJECT PERIOD THAT'S IN THE CALCULATION?

MS. BAUM: I'M GLAD THAT YOU MENTIONED THAT. SO AS DRAFTED, THAT'S WHAT WOULD TRANSPIRE. BUT I'LL TELL YOU IT'S VERY STICKY BUSINESS FIGURING OUT WHEN YOU CALCULATE THE PERIOD OF TIME FOR THE CREATION OF SOME INVENTION. I WANT TO SHARE WITH YOU THAT LAST WEEK WE WERE AT STANFORD, AND WE HAD A CALIFORNIA TECH TRANSFER-WIDE MEETING WHERE WE HAD REPRESENTATIVES FROM ALL THE TECH TRANSFER OFFICES. AND I BROUGHT THIS TO THEIR ATTENTION, AS I HAD EARLIER. AND THEY SAID, GEE, I DIDN'T REALLY UNDERSTAND WHAT THIS MEANT THE FIRST TIME WE WENT OUT. I SAID, LOOK, WE ARE SIMPLY GOING TO TRY TO INITIATE A RULEMAKING. IF YOU HAVE COMMENTS, WE'RE

HAPPY TO MEET WITH YOU, TALK TO YOU, AND WE CAN PROCEED TO FIGURE OUT WHAT THIS MEANS TO YOU.

I KNOW THAT THERE ARE CERTAIN BOARD MEMBERS HERE THAT THOUGHT IT WAS JUST THE PERIOD OF THE PROJECT PERIOD OF THE GRANT AWARD, AND THAT'S WHY IT WAS DRAFTED IN HERE.

SO WITH THAT SAID, I HAVE MADE COMMITMENTS TO THE HEAD OF TECH TRANSFER AT STANFORD AND THE CALIFORNIA OFFICE OF THE PRESIDENCY FOR THE UC'S TO MEET WITH THEM AND TALK FURTHER ABOUT THESE, AND WITH ANY BOARD MEMBERS THAT WANT TO JOIN IN THAT DISCUSSION.

SO LET ME JUST GO THROUGH THESE AND WE'LL SEE HOW FAR WE CAN GET. WE JUST NEED TO GET SOMETHING APPROVED SO THAT --

DR. STEWARD: CAN I ASK A CLARIFYING QUESTION? I KNOW THIS HAS BEEN DISCUSSED, AND I JUST DON'T REMEMBER THE ANSWER. THE TIMING, SO SOMETHING THAT HAPPENS DURING THE PERIOD OF THE GRANT IS WHAT QUALIFIES AND DETERMINES THE AMOUNT OF THE PERCENT. IS THAT THE TIME OF THE DISCOVERY OR THE TIME OF FIRST FILING?

MS. BAUM: I THINK WHAT YOU'RE ASKING IS WHAT IS THE DEFINITION OF INVENTION.

DR. STEWARD: THAT'S RIGHT.

MS. BAUM: SO THE DEFINITION OF INVENTION, WE HAVE A LOT OF DIFFERENT SCENARIOS, BUT I THINK IF IT'S CONCEIVED OUTSIDE, BUT REDUCED DURING THE PROJECT PERIOD, IT'S CONSIDERED A CIRM-FUNDED INVENTION, WHICH A LOT OF OUR MONEY IS GOING TO BE USED TO REDUCE TO PRACTICE OR TO GENERATE DATA. AND SO -- OR IF IT'S OBVIOUSLY CONCEIVED AND REDUCED TO PRACTICE WITHIN THE PROJECT PERIOD, IT'S A CIRM-FUNDED INVENTION AS WELL. OR IF IT'S CONCEIVED DURING THE PROJECT PERIOD AND REDUCED, I BELIEVE IT'S 12 MONTHS AFTER, SO THERE'S NO GAMING, THEN IT'S CONSIDERED A CIRM-FUNDED INVENTION. THOSE ARE THE THREE SCENARIOS THAT I RECALL WITHOUT HAVING IT IN FRONT OF ME OF HOW WE DEFINED THIS.

SO THAT'S JUST -- THIS IS NOT EASY. LET JUST GO THROUGH THE DIFFERENT SCENARIOS. I THINK IT'S REALLY IMPORTANT FOR BUSINESS THAT WE PROCEED WITH THESE SETS OF PROPOSED AMENDMENTS.

WE ALSO HAVE -- IT'S TOUGH. I KNOW. LOOKS LIKE THE PLANE WAS DELAYED OR SOMETHING IN A DREADFUL WAY. REMINDS ME OF OUR TRIP TO SAN DIEGO LAST WEEK.

THE SECOND GENERAL CONCEPT THAT WE'RE PROPOSING IS TO ALIGN OUR DEFINITION OF LICENSING REVENUE SIMILAR TO THE WAY WE'VE AGREED OR THE BOARD

AGREED TO DO. SO WITH RESPECT TO THE LOAN ADMINISTRATION POLICY, YOU MAY RECALL THAT A FEW MONTHS AGO THE ICOC AGREED THAT WITH RESPECT TO FOR-PROFITS, THAT PRECOMMERCIAL REVENUE WOULDN'T BE CONSIDERED REVENUE IN THE CONTEXT OF THE LAP. AND WE'RE SAYING IT SHOULDN'T BE CONSIDERED LICENSING REVENUE HERE WITH RESPECT TO FOR-PROFIT GRANTEES AND COLLABORATORS. THAT'S, IN ESSENCE, TO ALIGN THE SAME SORT OF THOUGHT PROCESSES FOR THE LAP AND APPLY THEM HERE. THE NOTION BEING THAT THOSE TYPES OF REVENUES ARE, IN ESSENCE, CONSIDERED IN THE INDUSTRY A PAYMENT IN ARREARS FOR FUNDING ALREADY INVESTED. AND WE WANTED TO MAKE THIS CHANGE AS WE DID IN THE LAP TO ELIMINATE ANY DISINCENTIVE TO ENGAGE IN CIRM. WE HEARD THAT WAS A BIG CONCERN WITH A LOT OF FOLKS.

THOSE ARE TWO KEY COMPONENTS OF CHANGES TO SECTION 100608 A. AND THEN WE HAVE A FEW MORE I WANT TO TALK TO YOU ABOUT WITH RESPECT TO THE REVENUE SHARING ARISING FROM THE OTHER INCOME STREAM, WHICH IS SALES FROM CIRM-FUNDED DRUGS, PRODUCTS, SERVICES. I THINK THIS IS THE PRIME IMPORTANCE AND WHAT OUR REAL GOAL WAS IN ADVANCING THESE SETS OF AMENDMENTS TODAY.

SO, FIRST OF ALL, WHAT WE WANTED TO DO, UNDER THE CURRENT REGULATIONS IT SAYS THAT -- I'M

SORRY NOT I'M ADVANCING MY SLIDES. I'M OBVIOUSLY VERY TIRED. I CAN DO IT. SO WHAT WE'RE TRYING TO DO HERE WITH RESPECT TO THIS CHANGE IS TO MAKE SURE THAT IT'S NOT THE GRANTEE OR THE COLLABORATOR THAT ULTIMATELY HAS TO PAY WHEN THEY COMMERCIALIZE A PRODUCT, BUT THAT WE'RE REACHING TO THE COMMERCIALIZING ENTITY. SO WE INTRODUCED THIS NEW CONCEPT, SAYING IT'S THE COMMERCIALIZING ENTITY THAT NEEDS TO PAY.

THE REASON TO DO THAT IS THAT ALTHOUGH, TECHNICALLY SPEAKING, WE COULD CREATE SYSTEMS WHERE THE GRANTEES AND COLLABORATORS WOULD HAVE TO PAY, THEY'RE TYPICALLY SORT OF THE MIDDLEMAN, THEY'RE THE SMALL BIOTECH THAT THEN WILL OFTEN WITH RESPECT TO DRUGS BE OUTLICENSING TO THE PHARMA. WHY NOT HAVE THE PHARMA PAY US DIRECTLY? THEN WE DON'T HAVE TO WORRY THAT THE MIDDLEMAN. THE SMALLER BIOTECH MIGHT NOT BE AROUND. SO WE MADE THAT CHANGE AND JUST CREATED THIS NEW DEFINITION.

THEN WHAT WE DID IS WE STATED THAT TO THE EXTENT THAT A COMMERCIALIZING ENTITY IS MAKING THE REQUIRED OR THE APPROPRIATE PAYMENT TO CALIFORNIA FOR THE SALE OF THE PRODUCTS, SERVICE, OR DRUG AS REQUIRED, THEN THE MIDDLE PERSON, THE MIDDLE ENTITY, SUCH AS THE GRANTEE OR COLLABORATOR IN CASE OF A

BIOTECH, WOULD NOT HAVE TO PAY ANY LICENSING REVENUE THAT'S DERIVED FROM THE SAME SALES REVENUE STREAM.

SO WHAT WE'RE TRYING TO SAY IS OR WHAT WE'RE TRYING TO ADDRESS IS THE SITUATION -- AS YOU CAN IMAGINE, YOU HAVE THE UC THAT THEN LICENSES TO A SMALL BIOTECH THAT THEN LICENSES TO A PHARMA COMPANY. SOMETIMES THE BIOTECH WILL ACTUALLY GET SOME MILESTONE PAYMENTS OR EVEN SOME ROYALTIES FROM THE PHARMA COMPANY. IF WE ARE OBTAINING A PAYMENT FROM THE PHARMA COMPANY, THEN WE'RE SAYING THAT WE SHOULDN'T COLLECT DOUBLE AND ALSO RECEIVE A PAYMENT FROM THE BIOTECH COMPANY.

AND, FINALLY, WHAT WE'RE SEEKING TO DO, AND THIS RELATES TO THE SMOOTHING OUT OF THE PAYMENT STREAMS, IS CHANGE THE ROYALTY PAYMENT AND SIMPLIFY IT AS WELL. SO WHAT WE CURRENTLY HAVE IS THAT A PAYMENT OF 3 PERCENT PER YEAR UNTIL YOU REACH THREE TIMES THE GRANT AMOUNT. AND THEN WE HAVE THIS ONETIME PAYMENT OF 3 X AT 250 MILLION REVENUES PER YEAR. AND THEN WE HAVE ANOTHER ONETIME PAYMENT OF 3 X ONCE YOU EXCEED $500 MILLION PER YEAR IN REVENUES, PLUS A 1-PERCENT ROYALTY AFTER THE 500 MILLION PER YEAR.

WHAT WE'RE TRYING TO DO IS ELIMINATE THESE ONETIME PAYMENTS BECAUSE THEY'RE CONSIDERED LUMPY.

AND TO SIMPLIFY IT, WE'VE OFFERED, AND THIS IS SOMETHING THAT WAS CONSIDERED IN-DEPTH BY THE IP AND INDUSTRY SUBCOMMITTEE, WE'VE OFFERED THIS ALTERNATIVE APPROACH. AND THAT IS THE ROYALTY RATE INSTEAD WOULD BE 0.1 PERCENT PER MILLION DOLLARS IN GRANTS. AND IT WOULD BE FOR THE EARLIER TO OCCUR OF TEN YEARS OR 9 X THE GRANT AMOUNT. AND THEN WE WOULD ALSO ON TOP OF THAT, ONCE THAT'S SATISFIED, HAVE THAT 1-PERCENT ROYALTY ON NET COMMERCIAL REVENUE IN EXCESS OF 500 HUNDRED MILLION A YEAR UNTIL THE LAST TWO EXPIRE PATENT COVERING A CIRM-FUNDED INVENTION. AND LIKE THE CURRENT LANGUAGE, THAT ADDITIONAL 1-PERCENT ROYALTY WOULD ONLY APPLY WHERE THERE WERE GRANTS IN EXCESS OR EQUAL TO OR IN EXCESS OF $5 MILLION FROM CIRM.

SO THOSE ARE THE FIVE GENERAL CONCEPTS THAT WE'RE TRYING TO FIND OR OBTAIN APPROVAL FROM THE BOARD FOR SO THAT WE CAN OPEN UP THIS PUBLIC COMMENT PERIOD. IF THERE'S ANYTHING THAT NEEDS TO BE ADDRESSED, ANY SORT OF CREATIVE WAYS, ESPECIALLY THAT THE NON-PROFITS WANT TO ADDRESS, WE CAN BRING THAT BACK TO THE BOARD.

AND IN DOING SO, THOUGH, I JUST WANT TO REMIND THE BOARD THAT WE NEED TO, IF WE APPROVE THESE AMENDMENTS, ALSO HAVE A SECOND MOTION BECAUSE

PURSUANT TO SB 1064, IF WE WANT TO CHANGE OUR REVENUE SHARING REQUIREMENTS, WE HAVE TO MAKE A CERTAIN FINDING WHICH IS ABOVE YOU ON THE SLIDE. AND THAT'S, IN ESSENCE, THAT THE AMENDMENTS WERE NECESSARY TO EITHER ENSURE ESSENTIAL RESEARCH IS NOT UNREASONABLY HINDERED AND/OR THAT THE STATE HAS AN OPPORTUNITY TO BENEFIT FROM PATENTS AND ROYALTIES IN ORDER TO ENSURE THAT THESE AMENDMENTS ARE BEING APPROVED.

MR. TORRES: SO MOVED ON THE FIRST AMENDMENT.

DR. JUELSGAARD: SECOND.

CHAIRMAN THOMAS: IT'S BEEN MOVED AND SECONDED. IS THERE DISCUSSION? MR. JUELSGAARD IS THE AUGUST COMMITTEE CHAIR. WOULD YOU LIKE TO COMMENT ON THIS PRESENTATION?

DR. JUELSGAARD: JUST REALLY BRIEFLY. SO WE ACTUALLY DID SPEND A FAIR AMOUNT OF TIME DISCUSSING THESE PARTICULAR ISSUES AT THE INTELLECTUAL PROPERTY AND INDUSTRY SUBCOMMITTEE. AND DUANE, WHO'S BEEN WAITING OUT IN THE LOBBY THE LAST THREE HOURS AND JOINED US NOW THAT THE CONTROVERSY IS DONE. ANYWAY, WE SPENT A LOT OF TIME DISCUSSING THIS AND REALLY RECKONING WHAT IN THE END WOULD WORK VIS-A-VIS INDUSTRY BECAUSE SOME OF THE

CONCEPTS THAT WERE EMBEDDED THERE JUST WERE NOT VERY WORKABLE, I THINK, FROM OUR COLLECTIVE POINT OF VIEW.

SO WE WERE PLEASED WITH THESE MODIFICATIONS THAT ARE BEING SUGGESTED TO BE MADE.

CHAIRMAN THOMAS: MR. HARRISON, THIS IS A VOICE VOTE ITEM, CORRECT?

MR. HARRISON: CORRECT.

CHAIRMAN THOMAS: ANY FURTHER DISCUSSION ON THIS PARTICULAR MOTION?

DR. LUBIN: SO I'M JUST CURIOUS. BEFORE AWARDS ARE MADE, IS THERE GOING TO BE A DOCUMENT DESCRIBING THIS THAT GOES TO THE INSTITUTION WHO SIGNS OFF ON AGREEING TO THESE PLANS?

MS. BAUM: THEY'RE OUR REGULATIONS. SO ONCE THEY'RE ENACTED, THEY -- BUT WE ALWAYS ENGAGE AND APPRISE THEM, AND WE'VE BEEN DOING THAT ALL ALONG.

MS. SAMUELSON: QUESTION. HOW ARE YOU GOING TO KNOW THAT THE ESSENTIAL RESEARCH IS NOT HINDERED OR THAT IT'S A REASONABLE AMOUNT OF HINDRANCE CONSIDERING THE STORIES WE'VE HEARD TODAY?

MS. BAUM: WHAT WE'RE ASKING, THAT IF YOU FIND THAT THESE AMENDMENTS ARE APPROPRIATE, WE ALSO ASK THAT YOU FIND THAT THEY'RE APPROPRIATE BECAUSE

WITHOUT THEM ESSENTIAL RESEARCH WOULD BE UNREASONABLY HINDERED OR THAT YOU FIND THAT THESE AMENDMENTS WILL ALLOW US OR CALIFORNIA TO BETTER BENEFIT FROM ROYALTIES AND PATENTS THAT ARE GENERATED FROM THE CIRM-FUNDED RESEARCH.

MS. SAMUELSON: THEY MAY SIGN OFF ON SOMETHING, BUT THEN A LAB MAY DECIDE NOT TO PURSUE A CERTAIN AREA BECAUSE THE ROYALTY HIT IS TOO HIGH. I DON'T HAVE THE STRENGTH OR ATTENTION SPAN NOW TO HAVE THE DISCUSSION. SO I SHOULDN'T EVEN OPEN MY MOUTH.

MY OTHER QUESTION IS HAS THIS BEEN NEGOTIATED OR LITIGATED OR SOMETHING WITH THE STATE PURSUANT TO THE PROVISIONS IN THE CURES ACT?

MS. BAUM: THERE'S NO LITIGATION ON THESE ISSUES IN TERMS OF NEGOTIATION. I THINK IF YOU MEAN THAT WE REGULARLY SEEK INPUT FROM STAKEHOLDERS, WE DO DO THAT.

MS. SAMUELSON: JUST GIVEN THERE'S PROVISION IN THE LAW FOR REVENUE SHARING AND THE CEILING ON DRUG COSTS. NEVER MIND. I WOULD THINK ALL OF THAT IS WORTHY OF DISCUSSION, BUT I CAN'T PURSUE IT NOW.

MR. ROTH: JOAN, MAYBE I CAN HELP. SO THERE'S TWO THINGS HERE. ONE, THERE'S SOME CHANGES

THAT WE THINK WILL IMPROVE THE IP POLICY THAT WE ORIGINALLY NEGOTIATED. SO THOSE ARE THE FIRST SET OF RECOMMENDATIONS. BUT IN ORDER --

MS. SAMUELSON: WITH THE STATE?

MR. ROTH: NO. NEGOTIATIONS WITH THE INSTITUTIONS AND THE POTENTIAL LICENSEES OF THESE INTELLECTUAL PROPERTY RIGHTS THAT MIGHT BE GENERATED. SO THAT WAS THE FIRST SET.

BUT IN ORDER FOR US TO TAKE THAT ACTION, WE'RE REQUIRED TO MAKE A FINDING THAT IF WE DIDN'T TAKE THAT ACTION, IT COULD IMPAIR RESEARCH FROM GOING FORWARD. SO IT'S JUST WE HAVE TO MAKE THAT FINDING IN ORDER TO MAKE THE CHANGE THAT WE'RE RECOMMENDING.

MS. SAMUELSON: OKAY.

CHAIRMAN THOMAS: OKAY. THE QUESTION HAS BEEN CALLED. ALL THOSE IN FAVOR OF THE MOTION ON THE TABLE PLEASE SAY AYE. OPPOSED? ABSTENTIONS? ANYBODY ON THE PHONE?

NOW, IS THERE A PART 2, IS THERE A SECOND THING?

MR. TORRES: YES. I SO MOVE.

MR. ROTH: SECOND.

CHAIRMAN THOMAS: PART 2 HAS BEEN MOVED BY THE SENATOR, SECONDED BY DUANE, WHICH IS, I ASSUME,

TWO LITTLE "I" THERE. ANY DISCUSSION ON THIS?

ACTUALLY WAS REMISS IN THE LAST SEGMENT AND FORGOT TO ASK IF THERE WAS ANY PUBLIC COMMENT. ANY PUBLIC COMMENT HERE? SEEING NONE, ALL THOSE IN FAVOR PLEASE SAY AYE. OPPOSED.

OKAY. IF WE CAN GET ONE MORE ITEM THROUGH, WE'LL BE DONE. SO LET'S GO TO ITEM NO. 19, CONSIDERATION OF THE AMENDMENTS TO THE STRATEGIC PARTNERSHIP FUNDING CONCEPT PLAN.

MS. BAUM: TODAY'S MY LUCKY DAY. ALL RIGHT. THIS TIME I ONLY HAVE ONE SLIDE. BUT YOU DO HAVE A BRIEFING, A MORE DETAILED DOCUMENT, WITHIN YOUR BINDERS. THANK YOU FOR YOUR CONSIDERATION AND FOR CONSIDERING THIS, PARTICULARLY AT THIS LATE HOUR.

AS YOU ALL KNOW, THE STRATEGIC PARTNERSHIP FUNDING PROGRAM IS NEW. WE HAVE LEARNED A LOT IN THE LAST FEW MONTHS. AND WHEN WE INITIALLY DRAFTED THIS PROPOSED CONCEPT, WE HAD SOME IDEAS OF HOW IT WOULD WORK. AND NOW THAT WE HAVE SOME TIME AND EXPERIENCE UNDER OUR BELTS, WE THINK WE CAN MAKE A LITTLE MORE TWEAKS TO MAKE IT WORK BETTER.

WHAT WE'RE PROPOSING TO DO IS THREEFOLD. IT'S PRETTY SIMPLE. FIRST, IT'S JUST A MECHANISTIC CHANGE. INITIALLY WE CALLED FOR A PROGRAM

ANNOUNCEMENT TO BE POSTED WITH SORT OF JUST A REVOLVING APPLICATION PROCESS. WE'RE CHANGING THAT A LITTLE TO REQUEST THAT IT JUST BE AN RFA THAT'S POSTED. WE HAVE IN OUR LONG-TERM PLANNING DETERMINED THAT WE WOULD SEEK TO POST EVERY SIX MONTHS. OF COURSE, DEPENDING ON THE BOARD REPLENISHING THE FUNDING, WHICH WE WILL BE COMING TO THE BOARD TO ASK FOR AT SOME POINT.

AND IN ADDITION, WHAT WE WANT TO DO IS NOT CHANGE THE OVERALL SCOPE OF WHAT WAS APPROVED FOR THIS PROGRAM, WHICH WAS BASIC RESEARCH ALL THE WAY TO PHASE II; BUT IN IMPLEMENTING IT, IT BECOMES VERY DIFFICULT TO MAKE SURE THAT WE CAN KEEP OUR VERY HIGH STANDARDS OF REVIEW IF WE NEED TO HAVE EXPERTS THAT COVER THAT FULL BODY OF RESEARCH PIPELINE FROM BASIC TO PHASE II.

SO WITH AN RFA-BY-RFA BASIS, WHAT WE'D LIKE TO DO IS HAVE THE ABILITY TO NARROW THE SCOPE AS APPROPRIATE.

AND, FINALLY, I GUESS I'M THE ONE WHO PLACED THE IP AND INDUSTRY SUBCOMMITTEE REVIEW WITHIN THE PROCESS AND HAVE COME TO REALIZE THAT THE TYPE OF DOCUMENTATION WE'RE GETTING WITH RESPECT TO COMMERCIAL VALIDATION IS NOT OF SUCH A COMPLICATED NATURE AND SO DETAILED THAT IT REQUIRES A REALLY

IN-DEPTH REVIEW BY, I THINK, THE SUBCOMMITTEE, AND IT CREATES A BURDENSOME AND AWKWARD SECONDARY STEP.

SO WHAT WE'RE PROPOSING TO DO IS LET THE ICOC CONSIDER THE EVIDENCE OF COMMERCIAL VALIDATION THAT'S PROVIDED ALONG WITH THESE APPLICATIONS. AND, OF COURSE, AS APPROPRIATE, CONSIDER THAT IN CLOSED SESSION WHEN THERE'S CONFIDENTIAL INFORMATION. AND INSTEAD OF THE IP AND INDUSTRY SUBCOMMITTEE, LET THE ICOC BE THE ENTITY THAT ULTIMATELY DECIDES WHEN WE WILL AGREE TO FUND MORE THAN THE AMOUNT ALLOTTED, IN THIS CASE, FOR STRATEGIC PARTNERSHIP I, IT WAS 10 MILLION, OR A LONGER TERM BECAUSE THE CURRENT PROPOSED CONCEPT PLAN SAYS THAT IT'S THE IP AND INDUSTRY SUBCOMMITTEE THAT DOES THE RECOMMENDATION FOR SUCH, BUT ULTIMATELY THE ICOC WOULD HAVE TO MAKE THAT FINAL DETERMINATION ANYWAY.

SO WHAT WE WANT TO DO AS PART OF THIS THIRD PROPOSED RECOMMENDED CHANGE IS TO ELIMINATE THE ROLE OF THE IP AND INDUSTRY SUBCOMMITTEE WITH REVIEW OF THE COMMERCIAL VALIDATION ASPECTS OF THIS PROGRAM. AND THEN, INSTEAD, HAVE THE ICOC DO IT. AND THAT'S THE SUM AND SUBSTANCE OF THESE PROPOSED CHANGES.

CHAIRMAN THOMAS: OKAY. THANK YOU, ELONA. I WOULD LIKE TO ADD WE'VE HAD A LOT OF DISCUSSION ON

THIS TOPIC IN EXECUTIVE COMMITTEE AS WELL. AND CURRENTLY, AND I'VE ALLUDED TO THIS, I THINK, AT LEAST TWICE AT PAST BOARD MEETINGS, WE ORIGINALLY AUTHORIZED 30 MILLION FOR THE PURPOSE OF THE STRATEGIC PARTNERSHIP FUND. IT IS OUR COLLECTIVE OPINION IN DISCUSSING THIS THAT SINCE THIS IS GOING TO BE A ROLLING RFA EVERY SIX MONTHS AND THAT WE'RE GOING TO HAVE EBBS AND FLOWS OF WHAT SEEM TO BE PROMISING PROJECTS THAT ARE UP FOR REVIEW, WITH RESPECT TO THE CURRENT ROUND, I THINK IF YOU WERE TO ASK DR. TROUNSON, HE WOULD TELL YOU THAT WE HAVE QUITE A NUMBER OF PROMISING PROJECTS OBVIOUSLY TOTALLY SUBJECT TO PEER REVIEW BY THE GRANTS WORKING GROUP. BUT BASED ON THE ANALYSIS THAT DR. TROUNSON AND COLLEAGUES HAVE DONE, IT IS MY RECOMMENDATION THAT WE FOR THIS SPECIFIC ROUND INCREASE THE AMOUNT TO BE AWARDED UP TO 60 MILLION AND THAT WE REVISIT THIS ON AN RFA-BY-RFA BASIS AS WE GO ALONG BASED ON WHAT WE'RE SEEING OUT THERE IN TERMS OF POTENTIAL PROJECTS. DR. TROUNSON, IS THAT A FAIR SUMMARY OF OUR DISCUSSION?

DR. TROUNSON: I THINK THAT'S A FAIR INDICATION OF THE POTENTIAL NEED. IF YOU REMEMBER, THAT WE WERE ONLY FUNDING UP TO $10 MILLION FOR EACH OF THE PROJECTS. AND SO I THINK IT WOULD BE OUR

ASSESSMENT THAT IT'S VERY LIKELY THAT SIX OR SEVEN GOOD PROJECTS MAY COME FORWARD IN THIS ROUND. WE DON'T KNOW WHAT WILL HAPPEN IN FUTURE ROUNDS, BUT IT'S LIKELY ALSO TO BE WELL ATTENDED TO BY THE BUSINESS SECTOR. SO I THINK IT WOULD BE VERY WISE TO CONSIDER THE POSSIBILITY, IF THE GRANTS WORKING GROUP RECOMMENDS, THAT WE HAVE A HIGHER NUMBER THAN THE 30 MILLION, AND 60 MILLION SOUNDS PRETTY REASONABLE.

MR. ROTH: J.T., I WANT TO SUPPORT THAT. I THINK WE NEED TO GIVE INDUSTRY A SIGNAL THAT THERE IS A PATHWAY TO GET FUNDED BY CIRM. AND I WASN'T HERE FOR THE DISCUSSION, BUT I HAD ENOUGH PHONE CALLS THIS WEEK TO KNOW THAT WE NEED TO DELIVER THAT MESSAGE. AND I THINK WE SHOULD MAKE SURE THEY UNDERSTAND THIS IS NOT A LIMITATION TO $30 MILLION. IF THERE ARE GOOD PROJECTS WITH GOOD SCIENCE THAT NEED TO BE FUNDED, WE HAVE SAID IT OVER AND OVER AGAIN, WE NEED TO INCREASE THAT AMOUNT. SO I SUPPORT WHAT YOU'RE TALKING ABOUT AND EVEN WOULD ENCOURAGE IT TO GO HIGHER.

MR. SHEEHY: I GUESS I HAD TWO POINTS. ONE IS I'M NOT SURE WE CAN DO THIS AT THIS MEETING BECAUSE WE HAVEN'T NOTICED THAT. BUT I WONDER IF IT MIGHT MAKE SENSE AS A WAY TO SEND A CLEAR SIGNAL IS

TO REALLOCATE THE UNUSED PORTION. I THINK IT WOULD BE WITHIN APPROPRIATE PROCESS TO REALLOCATE THE EXCESS FUNDS LEFT. WOULDN'T THAT BE PART OF CLOSING OUT THE DISEASE TEAMS? THAT WOULD ALMOST GET YOU TO YOUR SIXTY.

CHAIRMAN THOMAS: WE DON'T KNOW WHAT THE UNALLOCATED NUMBER IS SINCE WE STILL HAVE ONE ON THE TABLE.

MR. SHEEHY: WELL, NOTWITHSTANDING THAT, WE KNOW IT CAN'T BE LESS THAN 10 MILLION. JUST A SUGGESTION.

CHAIRMAN THOMAS: THANK YOU. MR. HARRISON, YOU KNOW WHERE WE'RE TRYING TO GET. WHAT IS YOUR OPINION ON THE BEST WAY TO PROCEED HERE?

MR. HARRISON: THE ITEM HAS BEEN AGENDIZED AS CONSIDERATION OF PROPOSED AMENDMENTS TO THE STRATEGIC CONCEPT PLAN. THOUGH THIS PARTICULAR AMENDMENT WAS NOT INCLUDED IN WHAT WAS PRESENTED TO THE BOARD IN ADVANCE IN WRITING, THE SUBJECT OF THE STRATEGIC FUNDING PARTNERSHIP CONCEPT PLAN WAS PROPERLY AGENDIZED. AND IT'S WITHIN THE BOARD'S DISCRETION TO CONSIDER MOTIONS THAT RELATE TO THAT ITEM.

CHAIRMAN THOMAS: OKAY. SO GIVEN THAT, WE NEED TO HAVE A --

DR. LEVIN: CAN I JUST ASK A QUESTION ON THIS? THE POINT OF RAISING THE CAP WOULD BE IN ORDER TO SEND THE GRANTS WORKING GROUP A MESSAGE THAT THEY HAVE UP TO $60 MILLION TO PLAY WITH IN GIVING THEIR RECOMMENDATIONS FOR FUNDING? OTHERWISE --

CHAIRMAN THOMAS: YES. AND ALSO TO GIVE INDUSTRY -- THIS ISN'T A NUMBER THAT WE'RE ARRIVING AT SORT OF ARBITRARILY. WE THINK THIS IS AN EDUCATED GUESS NUMBER, AND THAT IT SERVES THE DUAL PURPOSE OF DIRECTING THE GRANTS WORKING GROUP AND INDICATING TO INDUSTRY THAT THERE IS OPPORTUNITY OUT THERE FOR THE RIGHT PROJECTS.

DR. LEVIN: WE CAN PROBABLY MORE EFFECTIVELY COMMUNICATE BY WHEN THE GRANTS WORKING GROUP REVIEWS COME BACK AND WE SEE THEM, AND IF THEY ARE DEEMED MERITORIOUS, THEN WE ALWAYS HAVE THE AUTHORITY TO EXCEED THE CAP, WHATEVER WE SET IT AT, AND ACTUALLY AWARD THEM THE $60 MILLION. THAT'S PRETTY STRONG.

CHAIRMAN THOMAS: THAT IS AN OPTION. I PERSONALLY WOULD PREFER --

DR. TROUNSON: I WOULD ENCOURAGE THE BOARD TO GO ALONG WITH YOUR VIEW HERE, CHAIRMAN. I THINK IT'S ONE OF THE -- OUR STRATEGIC PLAN IS TO

ENCOURAGE INDUSTRY, AND WE WANT TO SEND THAT STRONG MESSAGE TO INDUSTRY, THAT WE'RE WILLING TO BE SUPPORTIVE. WE DID GET A LOT OF APPLICATIONS. WE WORKED HARD TO CONTRACT THEM INTO A DOABLE SIZE, AND THERE WERE 12 THAT WE INVITED FORWARD, AND THREE SEEMED A VERY SMALL NUMBER OUT OF THAT WHEN YOU THINK WHEN WE STARTED WITH 40.

SO I THINK THE IDEA THAT THE BOARD IS INTERESTED IN ENCOURAGING INDUSTRY, I THINK IT IS A PARTICULARLY GOOD MOVE. AND TO MAKE THAT PUBLICLY AWARE AS WE WOULD IF YOU GO AHEAD AND VOTE ON THIS. I THINK IT WOULD HELP US CONSIDERABLY IN OUR INTERACTIONS WITH INDUSTRY. AND I THINK THOSE PEOPLE WHO ARE IN INDUSTRY WOULD RECOGNIZE THAT.

CHAIRMAN THOMAS: MR. SHEEHY.

MR. SHEEHY: I WOULD BE WILLING TO MAKE THAT MOTION, BUT I WANT TO MAKE TWO OTHER POINTS. ONE, I WOULD LIKE TO TIE IT TO SOME -- JUST SO THAT WE SHOW THAT WE'RE ACTUALLY NOT JUST THROWING MONEY OUR LEFT AND RIGHT WIDELY, I WOULD LIKE TO TIE IT TO SOME POT OF UNUSED FUNDS. LIKE I BELIEVE THE EARLY TRANSLATION ROUND WAS SUBSTANTIALLY UNDER. I KNOW EVEN IF WE WERE TO APPROVE THIS GRANT, WE'D HAVE TEN -- EVEN IF WE WERE TO APPROVE THE FINAL GRANT, WE HAVE 10 MILLION OUT OF THIS ROUND. BUT I WOULD

LIKE TO SAY THAT FUNDS THAT WERE NOT EXPENDED IN EARLIER ROUNDS THAT WERE ALLOCATED BY THE BOARD ARE BEING REPURPOSED FOR THIS GRANT SO THAT WE'RE BEING FLEXIBLE, BUT WE'RE NOT MAKING NEW MONEY, SO TO SPEAK.

CHAIRMAN THOMAS: WE STILL HAVE ONE TABLED, HOWEVER.

MR. SHEEHY: DO WE KNOW WHAT WAS LEFT OVER OUT OF EARLY TRANSLATION? I THOUGHT WE WERE FAIRLY SUBSTANTIALLY UNDER BUDGET.

DR. OLSON: THERE WAS 25 MILLION LEFT OUT OF EARLY TRANSLATION. I'D JUST REMIND THE BOARD THAT SORT OF YOUR ABILITY TO FUND DIFFERENT PROGRAMS OBVIOUSLY DEPENDS ON WHAT YOU APPROVE IN CONCEPT GOING FORWARD BASED ON THAT. YES, AT THE MOMENT THERE WAS 25 MILLION LEFT OUT OF EARLY TRANSLATION.

MR. SHEEHY: SO THAT WOULD BE MY MOTION, TO TAKE THE 25 LEFT OVER. AND I DON'T THINK THAT'S A $20 MILLION GRANT. I THINK IT'S A $17 MILLION GRANT. SO FIVE FROM THE DISEASE TEAM ROUND AND APPLY THIS TOWARDS THIS.

I'D ALSO LIKE TO MAKE ONE OTHER POINT WHILE I HAVE THE FLOOR. THAT'S MY MOTION.

MR. TORRES: I THINK IT OUGHT TO BE DELAYED UNTIL WE DEAL WITH THE ISSUE TOMORROW.

MR. SHEEHY: THERE'S STILL 24 LEFT OVER.

MR. TORRES: IN THE PARKINSON'S?

MR. SHEEHY: THERE'S 25 FROM EARLY TRANSLATION, BUT WE STILL HAVE 24 MILLION IN THE DISEASE TEAM AS OF TONIGHT, SO THERE'S YOUR OTHER FIVE.

CHAIRMAN THOMAS: CAN I JUST ASK A CLARIFYING, MR. SHEEHY. WE HAD 24 LEFT OVER FROM EARLY TRANSLATION, BUT WHERE ARE WE PUTTING THE SIX MILLION WE JUST VOTED FOR FOR THE DUCHENNE EARLY TRANSLATION?

DR. SCHEINER: DISEASE TEAM.

CHAIRMAN THOMAS: THAT IS A DISEASE TEAM BUDGET NUMBER? HOW ARE WE ACCOUNTING FOR THAT?

DR. OLSON: AT THE MOMENT IT'S ACCOUNTED FOR IN THE DISEASE TEAM. OBVIOUSLY IT WILL BE AN EARLY TRANSLATION PROJECT. BUT IF YOU LOOK AT THE POT OF MONEY YOU HAVE LEFT AT THIS POINT WITH NOTHING ELSE APPROVED, YOU HAVE 52 MILLION IN UNALLOCATED FUNDS, OF WHICH ABOUT 25 WAS FROM THE EARLY TRANSLATION ROUND, AND THE BALANCE IS WHAT YOU HAVE NOT YET ADDRESSED IN THE CONTEXT OF THE DISEASE TEAM AWARDS.

MR. ROTH: JEFF, YOU CAN GO TO 60 MILLION.

CHAIRMAN THOMAS: THAT GETS YOU 30 TO GET

TO 60.

MR. SHEEHY: YEAH. SO THAT WOULD BE MY MOTION.

BUT THE OTHER -- SO I DO HAVE ANOTHER POINT ON THIS POLICY IF YOU WANT TO GET TO THAT.

CHAIRMAN THOMAS: IS YOUR MOTION YOU MOVE THE THREE PROPOSED AMENDMENTS WITH THAT AS AN ADDENDUM?

MR. SHEEHY: ACTUALLY SINCE WE'RE GOING TO AN RFA BASIS, I WOULD LIKE WHEN WE REAPPROVE FUNDS, I DON'T NEED TO SEE AN RFA, BUT I'D LIKE TO KNOW -- THIS WAS VERY BROAD FROM BASIC THROUGH PHASE II. SO I'D LIKE TO HAVE AN IDEA OF WHAT THE CONCEPT IS GOING TO BE WHEN WE PUT MONEY IN. SO I'D LIKE TO KNOW WHERE WE'RE FUNDING IN THE PIPELINE. IT'S JUST A LITTLE ADJUSTMENT BECAUSE YOU'RE GOING TO KNOW WHEN YOU COME TO US FOR MONEY. AND I JUST THINK THAT SHOULD BE PART OF WHAT WE APPROVE. I DON'T THINK THAT'S PROBLEMATIC, BUT JUST THAT ONE CLARIFICATION.

DR. FEIGAL: I WAS JUST GOING TO SAY IN OCTOBER WE'RE GOING TO BE COMING TO YOU WITH OUR THOUGHTS FOR STRATEGIC PARTNERSHIP II. SO YOU WILL HEAR.

MR. SHEEHY: THAT WAS JUST MY POINT. SO

WE'RE NOT JUST FILLING THE POT, BUT WE KNOW WE'RE GOING TO BE DOING, SAY, CLINICAL TRIAL WORK WHEN WE PUT THAT MONEY IN.

CHAIRMAN THOMAS: YES. WE WILL REVISIT THE AMOUNT WE WANT TO ALLOCATE PER ROLLING RFA EACH TIME TOWARDS YOUR POINT.

MR. SHEEHY: OKAY. THAT'S MY MOTION.

MR. ROTH: I'LL SECOND IT. YOU HAVE EVERYTHING IN THAT.

MR. SHEEHY: YEAH. I'M FINE WITH THAT.

CHAIRMAN THOMAS: MR. HARRISON, IF YOU WOULD LIKE TO TAKE A STAB AT WHAT THE MOTION IS.

MR. HARRISON: THE MOTION WOULD BE TO APPROVE THE PROPOSED AMENDMENTS TO THE STRATEGIC PARTNERSHIP PLAN AND CONCEPT PLAN AND INCREASE THE BUDGET UP TO 60 MILLION BY REALLOCATING UNUSED FUNDS FROM THE LAST EARLY TRANSLATION ROUND AND FIVE MILLION FROM THE DISEASE TEAM ROUND AND TO REVISIT THE BUDGET BEFORE EACH STRATEGIC PARTNERSHIP FUND RFA IS ISSUED.

CHAIRMAN THOMAS: VERY WELL SAID, MR. HARRISON. ANY DISCUSSION BY MEMBERS OF THE BOARD ON THIS? ANY COMMENTS BY MEMBERS OF THE PUBLIC? HEARING NONE, IS THIS A VOICE VOTE, MR. HARRISON, OR NOT?

MR. HARRISON: YES. IT'S A VOICE VOTE. IF WE COULD JUST GET A CLARIFICATION OF WHO THE SECOND WAS.

MR. ROTH: I SECONDED.

CHAIRMAN THOMAS: THE FRESHLY ENERGIZED DUANE ROTH.

MR. ROTH: I WAS REALLY OUT WATCHING THE DEMOCRATIC CONVENTION.

CHAIRMAN THOMAS: ALL THOSE IN FAVOR PLEASE SAY AYE. OPPOSED? ABSTAIN? MOTION CARRIES.

LADIES AND GENTLEMEN, THANK YOU FOR BEARING WITH US. WE WILL ADJOURN FOR THE MOMENT, RECONVENE AT 9 O'CLOCK TOMORROW MORNING SHARP. THANK YOU.

(THE MEETING WAS THEN CONCLUDED FOR THE EVENING AT 09:55 P.M.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

CROWNE PLAZA HOTEL
1177 AIRPORT BOULEVARD
BURLINGAME, CALIFORNIA
ON
SEPTEMBER 5, 2012

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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