BEFORE THE

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

REGULAR TELEPHONIC MEETING

LOCATION: AS INDICATED ON THE AGENDA

DATE: JULY 21, 2016
11 A.M.

REPORTER: BETH C. DRAIN, CSR
CSR. NO. 7152

BRS FILE NO.: 98786

I N D E X

JULY 21, 2016; 11 A.M.

CHAIRMAN THOMAS: THIS IS JON THOMAS HERE DOWN IN SAN DIEGO. I'D LIKE TO WELCOME EVERYBODY TO THE JULY MEETING OF THE ICOC AND APPLICATION REVIEW SUBCOMMITTEE. WE HAVE FOLKS ON THE LINE FROM A NUMBER OF DIFFERENT SPOTS; AND AS I UNDERSTAND IT, MEMBERS OF THE PUBLIC AT A NUMBER OF DIFFERENT SPOTS. SO LET'S PROCEED HERE. I GUESS WE CAN'T DO THE PLEDGE OF ALLEGIANCE SINCE WE'RE SPREAD OUT ALL OVER. SO, MARIA, IF YOU PLEASE CALL THE ROLL.

MS. BONNEVILLE: SURE. DAVID BRENNER.

KEN BURTIS.

DR. BURTIS: PRESENT.

MS. BONNEVILLE: ANNE-MARIE DULIEGE. HARV FEDEROFF. ELIZABETH FINI. MICHAEL FRIEDMAN. JUDY GASSON. DAVID HIGGINS.

DR. HIGGINS: HERE.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: HERE.

MS. BONNEVILLE: SHERRY LANSING. KATHY LAPORTE. BERT LUBIN. SHLOMO MELMED.

DR. MELMED: HERE.

MS. BONNEVILLE: LAUREN MILLER.

MS. MILLER: HERE.

MS. BONNEVILLE: LLOYD MINER. ADRIANA PADILLA.

DR. PADILLA: HERE.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: HERE.

MS. BONNEVILLE: ROBERT PRICE. FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. BONNEVILLE: ROBERT QUINT. DR. QUINT.

DR. QUINT: PRESENT.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: HERE.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: HERE.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: HERE.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: HERE.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: HERE.

MS. BONNEVILLE: KRISTINA VUORI. BRUCE WINTRAUB. DIANE WINOKUR.

MS. WINOKUR: HERE.

MS. CHEUNG: EXCUSE ME, MARIA. KATHY LAPORTE JUST JOINED AS WELL.

MS. BONNEVILLE: KATHY, ARE YOU ON THE LINE?

MS. LAPORTE: I SURE AM.

MS. BONNEVILLE: THANK YOU.

CHAIRMAN THOMAS: THANK YOU, MARIA. WE'LL PROCEED NOW TO ITEM NO. 3 ON THE AGENDA, WHICH IS CONSIDERATION OF APPLICATIONS SUBMITTED IN RESPONSE TO CLIN1: PARTNERING OPPORTUNITY FOR LATE STAGE PRECLINICAL PROJECTS AND CLIN2: PARTNERING OPPORTUNITY FOR CLINICAL TRIAL STAGE PROJECTS. I'M GOING TO TURN THE MEETING OVER TO MR. SHEEHY.

MR. SHEEHY: THANK YOU, J.T. SO IS DR. SAMBRANO GOING TO INTRODUCE THIS, OR DO WE HAVE SOMEONE ELSE FROM THE REVIEW TEAM WHO WILL INTRODUCE THESE PROJECTS?

DR. SAMBRANO: YES. THIS IS GIL, AND I WILL BE INTRODUCING ALL OF THE PROGRAMS.

MR. SHEEHY: SO SHOULD WE START WITH THE SUMMARY OF THE CLIN1-0671?

DR. SAMBRANO: YES. SO I'M GOING TO INTRODUCE THE PROGRAM AND WE WILL START WITH 0671.

I HAVE A SLIDE DECK THAT HAS BEEN MADE AVAILABLE FOR THOSE WHO ARE ON WEBEX. YOU CAN SEE IT, BUT I WILL TELL YOU IF SOMETHING IMPORTANT ON THESE SLIDES POP UP JUST SO YOU DON'T MISS ANYTHING.

SO ON THE FIRST SLIDE THAT I'M SHOWING IS JUST THE CLINICAL STAGE PROGRAM, A REMINDER THAT FOR THIS PROGRAM WE ACCEPT APPLICATIONS FOR IND-ENABLING WORK, CLINICAL TRIAL, AS WELL AS FOR SUPPLEMENTAL ACTIVITIES FOR CLINICAL TRIALS AND IND-ENABLING WORK.

TODAY WE'RE CONSIDERING TWO APPLICATIONS, ONE UNDER THE CLIN1 PROGRAM AND ANOTHER UNDER THE CLIN2 PROGRAM.

ON THE NEXT SLIDE IS A REMINDER OF THE SCORING SYSTEM THAT WE UTILIZE FOR OUR CLINICAL PROGRAM. A SCORE OF 1, 2, OR 3 WHERE A SCORE OF 1 MEANS THAT THE APPLICATION HAS EXCEPTIONAL MERIT AND WARRANTS FUNDING. A SCORE OF 2 MEANS THAT THE APPLICATION NEEDS IMPROVEMENT, DOES NOT WARRANT FUNDING AT THIS TIME, BUT COULD BE RESUBMITTED TO ADDRESS THOSE AREAS FOR IMPROVEMENT. AND THEN, FINALLY, A SCORE OF 3 MEANS THAT THE APPLICATION WAS DEEMED TO BE SUFFICIENTLY FLAWED THAT IT WOULDN'T WARRANT FUNDING AND CANNOT BE RESUBMITTED FOR AT LEAST SIX MONTHS. SO THAT IS THE SCORING SYSTEM.

AND THE FIRST APPLICATION UNDER CONSIDERATION IS CLIN1-08671. THIS IS AN APPLICATION FOR PRECLINICAL DEVELOPMENT OF A CELL THERAPY AND A DEVICE FOR DIABETES. THE THERAPY

INVOLVES HUMAN EMBRYONIC STEM CELL-DERIVED PANCREATIC PROGENITOR CELLS THAT ARE DELIVERED VIA A DEVICE, THAT, UNLIKE A PREVIOUS DEVICE THAT WAS UTILIZED, ALLOWS FOR DIRECT VASCULARIZATION.

THE INDICATION IS FOR HIGH RISK TYPE 1 DIABETES PATIENTS INCLUDING THOSE WITH BRITTLE DIABETES AND HYPOGLYCEMIA UNAWARENESS. THE GOAL, OF COURSE, IS TO COMPLETE PRECLINICAL RESEARCH ACTIVITIES THAT WOULD BE NEEDED TO SUBMIT AN IND AND THEN SUPPORT A FUTURE CLINICAL TRIAL.

THE MAJOR ACTIVITIES ARE RELATED TO MANUFACTURING AND QUALITY CONTROL OF THE CELLS AND DEVICES, TO CONDUCT A PRECLINICAL SAFETY STUDY WITH THE NEW DEVICES IN PARTICULAR, AND TO PREPARE AND SUBMIT AN IND TO THE FDA TO ALLOW FOR CLINICAL TESTING.

THE FUNDS REQUESTED IS ABOUT 3.9 MILLION. THERE IS CO-FUNDING THAT IS PROVIDED BY THE APPLICANT.

ON THE NEXT SLIDE, I'LL SHOW THE OUTCOME OF THE REVIEW. AS ALWAYS FOR CLINICAL PROGRAMS, WE CONDUCT A BUDGET REVIEW, AND THE APPLICATION PASSED THE BUDGET REVIEW TO ENSURE THAT ALL COSTS ARE, IN GENERAL, WITHIN SCOPE AND ARE REASONABLE.

THE GRANTS WORKING GROUP THEN REVIEWED THE

APPLICATION. THIS PARTICULAR APPLICATION WAS REVIEWED TWICE, BUT IN THE LAST REVIEW RECEIVED A SCORE OF 1. THERE WERE SIX VOTES OF THE MEMBERS VOTING FOR A SCORE OF 1, FOUR FOR A SCORE OF 2, AND THREE THAT GAVE IT A SCORE OF 3. THE CIRM TEAM ALSO EXAMINED THE PROCESS AND THE PROPOSALS TO ENSURE THAT THE APPLICATIONS MEET WHAT WE ARE LOOKING FOR AND THAT THE PROCESS WAS DONE IN AN APPROPRIATE WAY. AND AS SUCH, WE CONCUR WITH THE RECOMMENDATION OF THE GRANTS WORKING GROUP TO AWARD 3.9 MILLION TO THIS APPLICANT.

SO AT THIS POINT I GUESS WE CAN PAUSE AND CONSIDER THIS PROPOSAL. MR. SHEEHY.

MR. SHEEHY: THANK YOU, DR. SAMBRANO. SO DO I HAVE A MOTION TO EITHER ACCEPT OR NOT ACCEPT THE RECOMMENDATION OF THE GRANTS WORKING GROUP?

MR. TORRES: MOVE TO ACCEPT.

DR. PRIETO: I'LL SECOND.

MR. SHEEHY: SO IT'S MOVED BY SENATOR TORRES AND SECONDED BY DR. PRIETO. DO WE HAVE DISCUSSION? DOES ANY MEMBER OF THE COMMITTEE WISH TO COMMENT, ASK QUESTIONS, ETC.?

DR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD. CAN YOU HEAR ME?

MR. SHEEHY: YES, I CAN.

DR. JUELSGAARD: SO I DO HAVE A QUESTION OF DR. SAMBRANO. SO WHEN I LOOK AT THE SCORING -- YOU'RE GOING TO HAVE TO REMIND ME OF HOW THE SCORING WORKS BECAUSE, TO BE HONEST WITH YOU, I'VE FORGOTTEN. I APOLOGIZE FOR THAT IN ADVANCE. BUT WHEN I LOOK AT THE SCORING, WE HAVE 13 PEOPLE WHO SCORED THIS. SIX OUT OF THE 13 OR LESS THAN 50 PERCENT SCORED IT A 1. WE THEN HAD FOUR THAT SCORED IT AS, WELL, MAYBE BRING IT BACK AGAIN WITH SOME CLEANUP AND WE'LL LOOK AT IT. YOU CAN BRING IT BACK AGAIN AFTER SIX MONTHS IF YOU WANT TO AND WE CONSIDER WHAT YOU'RE DOING.

SO THE WAY I READ THIS IS WE HAVE, IN ESSENCE, SIX THAT SAY, YES, LET'S GO TODAY AND SEVEN THAT SAY, WELL, WAIT A MINUTE, HANG ON, WE MAY BE ABLE TO GO WITH THIS BUT NOT RIGHT NOW. SO HOW DOES THIS SCORING WORK THAT WE DERIVE A 1 FROM THE WAY THE BREAKUP OF THE SCORES ARE?

DR. SAMBRANO: SURE. THE WAY WE DO THIS IS BASED ON A PLURALITY OF MEMBERS. SO FOR A SCORE OF 1 OR A SCORE OF 2, A PLURALITY VOTE OF THE MEMBERS IS WHAT DETERMINES THE SCORE. FOR A SCORE OF 3, THERE'S A MAJORITY THAT IS REQUIRED. AND PART OF IT WAS THAT PREVIOUSLY YOU MIGHT RECALL THAT THAT WAS KIND OF A DON'T COME BACK SCORE, AND THAT'S WHY

WE REQUIRED A MAJORITY FOR A SCORE OF 3.

AND BECAUSE THERE ARE THREE CATEGORIES, AS IN THIS EXAMPLE, THERE ARE OFTEN CASES WHERE YOU'RE NOT GOING TO HAVE A CLEAR MAJORITY. AND THAT'S THE REASON, IN GENERAL, THAT WE WENT WITH A PLURALITY THAT DETERMINES THE SCORE. AND YOU CAN VIEW IT A COUPLE OF WAYS. THE VOTES FOR A SCORE OF 2 ARE PERHAPS AMBIVALENT, BUT THEY DO SUGGEST THAT THE APPLICATION, AT LEAST IN THE OPINION OF REVIEWERS, HAS MERIT. AND AS YOU SAID, THERE MAY BE SOME THINGS THAT NEED TO BE CLEANED UP, BUT OTHERWISE IS MERITORIOUS. SO TEN VERSUS THREE THAT FEEL THAT IT HAS MERIT OR SIX VERSUS SEVEN IN TERMS OF WHETHER IT SHOULD BE FUNDED RIGHT NOW. BUT THE SCORE IS CARRIED BY A PLURALITY OF VOTES.

DR. JUELSGAARD: ALL RIGHT. I'M NOT SURE IF WE HAD THIS PARTICULAR SITUATION. AND I'LL JUST SAY THIS AND THEN LEAVE IT AT THAT. IT JUST SEEMS ODD THAT WE HAVE SEVEN PEOPLE OUT OF 13 WHO BELIEVE THAT IT ISN'T QUITE READY FOR PRIME TIME AND ONLY SIX OF THE 13 WHO BELIEVE IT DOES. AND SO DID THE PEOPLE WHO SCORED IT 2 UNDERSTAND THAT THEIR SCORES EFFECTIVELY ARE GOING TO BE BUMPED UP TO 1 ALONG THE WAY?

DR. SAMBRANO: WELL, THEIR SCORES ARE NOT

BUMPED UP. IT'S JUST THAT IT'S THE PLURALITY OF THE MEMBERS THAT DRIVE THE SCORE. AND THEY DO UNDERSTAND. WE EXPLAIN THE RULES BEHIND WHAT DETERMINES THE FINAL SCORE, AND IN THIS CASE THAT IT WAS THE PLURALITY THAT DETERMINED THE SCORE FOR THIS ONE.

DR. MELMED: COULD I EXTEND THAT QUESTION? I EXTEND THAT QUESTION? IS IT POSSIBLE FOR THE COMMITTEE TO HEAR WHAT THE CONCERNS OF THE THREE 3S WERE? WHAT ARE THE CONCERNS BECAUSE THIS IS $4 MILLION. IT'S A SIZABLE GRANT. AND IF THERE WERE SEVEN PEOPLE WHO ARE VOTING AGAINST FUNDING NOW, I THINK IT WOULD HELP THIS COMMITTEE IF WE HEARD WHAT THOSE CONCERNS WERE ESPECIALLY FOR THOSE WHO GAVE IT A 3.

DR. SAMBRANO: SO THE SUMMARY THAT WE PROVIDED HAS AN OVERVIEW OF BOTH THE STRENGTHS AND THE WEAKNESSES OF THIS APPLICATION. AND THERE WERE A COUPLE OF REVIEWS THAT THIS APPLICATION WENT THROUGH. SO SOME OF THE CONCERNS RELATED TO THE RATIONALE FOR UTILIZING THIS PERFORATED CAPSULATION DEVICE VERSUS THE ORIGINAL DEVICE THAT HAS BEEN AND CONTINUES TO BE TESTED.

I THINK ULTIMATELY THE REVIEWERS FELL ON THE SIDE THAT THEY WANTED TO GIVE AN OPPORTUNITY TO

THE APPLICANTS TO TRY AND CONDUCT SOME OF THE PRECLINICAL ACTIVITIES, ESPECIALLY THE SAFETY AND TUMOROGENICITY STUDIES, TO ASSESS WHETHER THIS NEW DEVICE WOULD HOLD PROMISE AND ULTIMATELY BE ABLE TO SUPPORT A CLINICAL TRIAL.

I THINK THERE WAS DOUBT AMONG THE REVIEWERS WHETHER THAT WOULD END UP BEING THE CASE, BUT ULTIMATELY THEY FELT THAT IT WAS IMPORTANT TO AT LEAST GIVE IT A CHANCE.

DR. MELMED: CAN I INTERRUPT? SIX FELT THAT, BUT SEVEN DIDN'T.

DR. SAMBRANO: NO. I CAN'T TELL YOU WHAT EACH INDIVIDUAL FELT. ALL I CAN EXPLAIN IS WHAT THE SENSE OF THE GROUP AS A WHOLE WAS. SO THERE WERE COMMENTS THAT WERE PROVIDED BY MANY OF THESE REVIEWERS THAT IN GENERAL WERE FAVORABLE, BUT ALSO THAT EXPRESSED SOME CONCERN. AND ULTIMATELY SOME FELL ON THE SIDE OF WE FEEL, GIVEN WHAT WE'VE HEARD AND WHERE WE ARE, THAT THIS IS SOMETHING THAT SHOULD BE FUNDED NOW. THERE WERE FOUR THAT FELT, WELL, MAYBE THEY CAN TWEAK THIS, AND THREE THAT FELT, WELL, I DON'T FEEL THAT THIS IS SOMETHING THAT WE CAN FUND NOW. BUT BEYOND THAT, I REALLY CANNOT SPEAK TO EACH INDIVIDUAL VIEW.

DR. MELMED: THANK YOU.

MR. SHEEHY: DO WE HAVE OTHER COMMENTS AND QUESTIONS? SO THERE'S PUBLIC AT SOME SITES. ARE THERE ANY MEMBERS OF THE PUBLIC WHO WISH TO SPEAK TO THIS APPLICATION? OKAY. IS THERE SOMEONE WHO WISHES TO MAKE PUBLIC COMMENT?

MS. CHEUNG: NOT IN OAKLAND.

DR. DULIEGE: JEFF, THIS IS ANNE-MARIE DULIEGE. I'M SORRY. I HAD A QUESTION ACTUALLY.

MR. SHEEHY: PLEASE DO.

DR. DULIEGE: I JUST WANT TO HEAR FROM THE STAFF AT CIRM WHAT IS THE ALTERNATIVE IF WE DECIDE THAT STILL THERE'S SUFFICIENT CONCERN THAT IT NEEDS FURTHER REVIEW, THEY WERE NOT FULLY SUPPORTIVE OF GRANTING THIS GRANT? WHAT WILL BE THE CONSEQUENCES FOR THE APPLICANTS? OBVIOUSLY THEY WON'T GET THE MONEY, BUT WHAT CAN THEY DO? CAN THEY REPROCESS THEIR APPLICATION, ADDRESSING SOME OF THE REMAINING CONCERNS.

DR. SAMBRANO: THEY COULD. SO IF YOU DECIDE THAT THIS REALLY IS AN APPLICATION THAT SHOULD NOT BE FUNDED NOW, AND, JAMES, YOU CAN HELP ME IN TERMS OF WHETHER THIS COMMITTEE CAN ASSIGN IT A SCORE OF 2 AND, THEREFORE, ALLOW IT TO RESUBMIT, OR A SCORE OF 3, OR WHETHER THE DECISION IS SIMPLY JUST TO NOT FUND. BUT EITHER WAY, THEY WOULD HAVE

THE OPPORTUNITY TO COME BACK.

MR. HARRISON: GIL, IN RESPONSE TO THAT QUESTION, THE COMMITTEE COULD DECIDE TO ASSIGN A SCORE OF 2 IF IT WISHED.

DR. DULIEGE: OKAY.

CHAIRMAN THOMAS: QUESTION FOR GIL. JUST TO REITERATE, IT IS THE TEAM'S RECOMMENDATION THAT THIS PROPOSAL BE APPROVED?

DR. SAMBRANO: IT IS.

CHAIRMAN THOMAS: THANK YOU.

DR. PRIETO: IS IT APPROPRIATE FOR ME TO COMMENT ON THE DISCUSSION AT THE GWG SINCE I PARTICIPATED IN THAT REVIEW?

MR. SHEEHY: YEAH. IT'S ABSOLUTELY APPROPRIATE.

DR. PRIETO: OKAY. SO I THINK MAYBE I CAN SHED A LITTLE BIT OF LIGHT ON THIS. THIS IS AN APPLICANT THAT WE HAVE FUNDED SIGNIFICANTLY UP TO THIS POINT AND WHO IS IN CLINICAL TRIALS ALREADY. AND IN THOSE CLINICAL TRIALS THEY ENCOUNTERED, AND I THINK MOST OF YOU ARE PROBABLY FAMILIAR WITH THE BASIC TECHNOLOGY HERE, THIS IS A HUMAN EMBRYONIC STEM CELL APPLICATION, A DEVICE THAT IS IMPLANTED INTO PEOPLE WITH SEVERE TYPE 1 DIABETES. THEY ENCOUNTERED SEVERAL OBSTACLES TO ENGRAFTMENT IN SOME

OF THEIR INITIAL SUBJECTS AND ARE LOOKING AT SEVERAL APPROACHES TO TRY TO IDENTIFY, AND MAYBE GIL CAN CORRECT ME IF I'M MISSTATING THIS, BUT WHERE THE EXACT BARRIERS ARE.

THEY HAVE SOME INDICATIONS FROM THEIR PRELIMINARY RESULTS THAT THIS OR THAT MAY BE THE BARRIER TO ENGRAFTMENT, AND A SUBJECT WHO HAS HAD ENGRAFTMENT AND, OF COURSE, ALL OF THIS IS ONGOING AND VERY EARLY WORK, BUT THEY ARE LOOKING AT VARIOUS APPROACHES TO OVERCOME THAT AND ACHIEVE ENGRAFTMENT OF THEIR DEVICE NOW OF THE CELLS.

SOME OF THE MEMBERS OF THE WORKING GROUP ARE SKEPTICAL ABOUT THE POTENTIAL FOR SUCCESS FOR SOME OF THEIR SUGGESTED SOLUTIONS. I THINK A MAJORITY OF THEM, AS EVIDENCED BY THE VOTE, THINK THAT THE IDEA DEFINITELY HAVE -- THAT THEIR IDEAS HAVE MERIT. THERE WAS A DIFFERENCE OF OPINION ABOUT THIS OR THAT POTENTIAL SOLUTION AND HOW VIABLE THAT MIGHT BE. MY FEELING IS THAT UNLESS WE ALLOW THEM TO DO THE WORK AND CONTINUE TO TRY TO SOLVE THESE PROBLEMS, WE WON'T HAVE ANY WAY OF KNOWING THE ANSWER AND KNOWING WHAT IS THE -- HOW DO YOU OVERCOME THE BARRIER.

DR. DULIEGE: THANK YOU. THAT'S VERY HELPFUL.

MR. SHEEHY: DO WE HAVE OTHER QUESTIONS OR COMMENTS?

MR. PANETTA: JEFF, THIS IS JOE PANETTA. I JUST WANT TO FOLLOW UP ON THAT SO THAT I CAN BETTER UNDERSTAND WHERE THIS MIGHT PLACE US IF WE CHOOSE TO GO DOWN AN ALTERNATIVE PATH. IF I UNDERSTAND THIS APPLICATION AND REMEMBER IT, WE'VE MADE A VERY, VERY SIGNIFICANT INVESTMENT IN THIS APPLICANT UP TO THIS POINT OVER THE COURSE OF A NUMBER OF YEARS. AND IT SOUNDS AS THOUGH WE'RE AT A POINT NOW WHERE IF WE GO WITH THE RECOMMENDATION TO ADOPT THIS NEW APPROACH, THAT THIS COULD POTENTIALLY HELP TO GET THIS APPLICANT FURTHER DOWN THE ROAD TOWARD ACCOMPLISHING THE GOALS THAT WE HOPE THEY CAN ACCOMPLISH THROUGH ALL THE INVESTMENT THAT WE'VE MADE. IF WE DON'T, DO WE SEND THEM BACK TO THE DRAWING BOARD? ARE THEY STOPPED DEAD IN THEIR TRACKS? WHERE DOES THIS PLACE US?

MR. SHEEHY: RIGHT NOW THE MOTION WE HAVE ON THE FLOOR IS TO APPROVE THIS APPLICATION. THE ALTERNATIVE, AND I'M GOING INTUIT FROM KIND OF THE DISCUSSION AND FROM WHAT JAMES SAID, IS THAT ONE ALTERNATIVE MIGHT BE THAT WE VOTE DOWN THIS MOTION OR A NEW MOTION GETS SUBSTITUTED THAT AWARDS THIS A 2. IF IT GETS AWARDED A 2, THEN IT GOES BACK TO THE

WORKING GROUP AND TO THE APPLICANT FOR THE APPLICANT TO RESUBMIT TO TRY TO BETTER ADDRESS THE CONCERNS THAT WERE EXPRESSED BY THE REVIEWERS WHO GAVE IT A 2. DOES THAT MAKE SENSE?

MR. PANETTA: YEAH, IT DOES. I'M JUST -- I'M QUESTIONING IT MORE -- AND THAT'S A GREAT EXPLANATION. THANKS. I'M QUESTIONING IT MORE BECAUSE IT SOUNDS AS THOUGH, FROM WHAT I JUST HEARD, IF THE APPLICANT ADOPTS THIS APPROACH, THE IDEA BEHIND ADOPTING THIS APPROACH IS TO TRY TO GET AROUND WHAT SOUNDS LIKE A DIFFICULTY THAT THEY'RE ENCOUNTERING IN THE CURRENT APPROACH THAT THEY'RE TAKING. AND MAYBE THIS IS A DISCUSSION FOR LATER ON IF WE DECIDE TO GO DOWN THAT ROAD, BUT I'M TRYING TO BETTER UNDERSTAND WHAT ALTERNATIVE THEY MIGHT HAVE TO GO BACK AND IMPROVE THIS APPLICATION BECAUSE WHAT I THOUGHT I HEARD WAS THAT SOME PEOPLE WERE SKEPTICAL THAT THIS APPROACH MIGHT NOT WORK.

MR. SHEEHY: MAYBE FRANCISCO CAN CORRECT ME IF I MISS A POINT OR TWO. I THINK THAT THEY ARE TRYING TO MODIFY THIS, AS DR. PRIETO SAID, TO GET BETTER ENGRAFTMENT. AND PART OF WHAT'S BEING CONTEMPLATED HERE IS GOING INTO A SICKER POPULATION. SO THERE ARE TWO PARTS TO IT. AND SO IT DOES FEEL AS THOUGH IT'S A LITTLE BIT HIGH RISK KIND OF

APPROACH, BUT ALSO THAT RISK IS BEING BALANCED BY GOING INTO POTENTIALLY A HIGHER -- A GREATER NEED POPULATION.

AND I THINK THAT, AS FRANCISCO SAID, THIS IS REALLY ABOUT THE PRECLINICAL WORK TO REALLY DETERMINE IF THIS APPROACH HAS ANY MERIT AT ALL. AND I THINK THE PEOPLE WHO VOTED TO PUT THIS FORWARD SAID, YOU KNOW, THIS IS A HIGH RISK, POTENTIALLY HIGH REWARD TYPE OF EXPERIMENTS THAT ARE GOING TO TAKE PLACE, BUT THERE WERE PEOPLE WHO THOUGHT THAT THE EXPERIMENTS MIGHT NOT SUCCEED AND THAT THAT WAS KIND OF THE PUSH AGAINST IT. AM I CORRECT ON THAT, FRANCISCO? IS THAT KIND OF CAPTURING WHAT THE DISCUSSION WAS?

DR. PRIETO: YES. I THINK THAT DOES CAPTURE IT. AND I THINK THIS IS ONE OF, BUT NOT THE ONLY APPROACHES THAT THIS APPLICANT IS LOOKING AT TO OVERCOME THE BARRIERS THAT THEY'RE SEEING. THERE WAS SOME SKEPTICISM ABOUT THIS PARTICULAR ONE AND DISCUSSION ABOUT, WELL, I DON'T KNOW IF YOU WANT TO SAY MORE DRASTIC, BUT IT DOES IN INVOLVE SOME OTHER STEPS AND ISSUES FOR THE PEOPLE WHO WOULD BE INVOLVED IN A CLINICAL TRIAL IF THIS GOES FORWARD, BUT THAT WAS PART OF THE RATIONALE FOR USING A SICKER OR MORE SEVERELY AFFECTED POPULATION.

MR. PANETTA: THANKS.

MR. SHEEHY: SO DO WE HAVE MORE QUESTIONS, COMMENTS?

DR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD. SO TWO. THE FIRST IS THE FUNDS REQUESTED ARE CLOSE TO $4 MILLION, AND THERE'S CLOSE TO A MILLION DOLLARS IN CO-FUNDING. AND, AGAIN, THIS IS JUST TRYING TO REMEMBER WHAT KIND OF THE RULES OF THE ROAD ARE HERE. SO I TAKE IT THAT A ONE FOR FOUR CO-FUNDING IS ACCEPTABLE IN THIS SITUATION; IS THAT RIGHT?

DR. SAMBRANO: YES, IT IS. THE AMOUNT OF CO-FUNDING THAT IS PROVIDED IS WHAT IS REQUIRED OF FOR-PROFIT APPLICANTS AT THIS STAGE OF DEVELOPMENT.

DR. JUELSGAARD: OKAY. AND THEN THE SECOND THING IS, WE DO THIS, I KNOW, FROM TIME TO TIME, THE QUESTION IS I KNOW YOU GUYS CREATE MILESTONES AS THINGS MOVE FORWARD THAT PEOPLE HAVE TO MEET; AND IF THEY DON'T MEET THEM OR MEET THEM IN A TIMELY MANNER, THEN THAT KIND OF BRINGS EVERYTHING TO A HALT. SO THE QUESTION IS, AND I COME BACK TO THE FACT THAT I STILL SEE THIS AS A SEVEN TO SIX VOTE NOT IN FAVOR OF PROCEEDING, JUST FROM A GWG POINT OF VIEW, FORGET ABOUT OUR PLURALITY APPROACH FOR A MOMENT. THAT'S JUST A LITTLE TROUBLING TO ME,

AND MAYBE WE COULD TAKE THIS ISSUE BACK UP OF HOW WE COUNT THOSE AT A MEETING AT THE NEXT BOARD MEETING OR WHATEVER, BUT LET'S PUT THAT ASIDE BECAUSE THIS IS THE RULES THAT WE HAVE NOW.

SO IS THERE A WAY OF BUILDING A MILESTONE, THAT IF THEY DON'T ACHIEVE CERTAIN THINGS THAT ARE CRITICAL HERE, WE KIND OF CLOSE THE DOOR ON SPENDING ANY MORE MONEY?

DR. SAMBRANO: YES. ABSOLUTELY. SO THAT IS PART OF THE PROCESS THAT WE ENGAGE IN WITH ALL APPLICANTS AND ALL GRANTEES. AND IT'S ONE OF THE FIRST STEPS THAT WE TAKE WHEN FUNDING IS APPROVED BY YOU. SO WHEN THAT HAPPENS, WE GET TOGETHER WITH THE GRANTEE TO BE AND DEFINE SPECIFIC OPERATIONAL MILESTONES TO ENSURE THAT THEY CAN ACHIEVE THE GOALS OF THE PROPOSAL. AND WE ALSO MONITOR AND CAN MANAGE DISBURSEMENT OF FUNDS APPROPRIATELY.

DR. JUELSGAARD: GREAT. OKAY.

MR. SHEEHY: SO DOES THAT ANSWER YOUR QUESTION, STEVE?

DR. JUELSGAARD: YES, IT DOES. YES. THANK YOU.

MS. LAPORTE: THIS IS KATHY. DO WE HAVE ANY SENSE IN THAT REGARD OF WHAT'S THE LIKELIHOOD THAT WE'LL KNOW WHETHER THEY'RE HITTING THIS ON THE

FIRST MILLION DOLLARS OR SOME PROJECTS UNFORTUNATELY TAKE (INAUDIBLE)? DO YOU HAVE A READ ON IT?

DR. SAMBRANO: I REALLY CAN'T SAY OR HAVE A READ ON EXACTLY WHEN OR HOW MUCH IT WOULD TAKE. I MEAN THEY HAVE LAID OUT IN A CHART WHAT THE PROPOSED ACTIVITIES ARE THAT ENTAIL MANUFACTURING, DOING SOME OF THE PRECLINICAL WORK. MANY OF THE STUDIES OR AT LEAST SOME OF THE STUDIES ARE STARTING EARLY ON, SOME ARE BEGINNING NEAR THE MIDDLE OF THE TWO-YEAR AWARD TIME, AND THEY ALSO HAVE PARALLEL WORK THAT'S GOING ON. SO IT WOULD BE DIFFICULT FOR ME TO KNOW OR TO SAY WHERE IT IS THAT THEY MIGHT MOST LIKELY RUN INTO DIFFICULTIES FOR THIS ONE.

MR. SHEEHY: DOES THAT ANSWER YOUR QUESTIONS, KATHY?

MS. LAPORTE: YES. THANKS.

MR. SHEEHY: ADDITIONAL QUESTIONS OR COMMENTS? AGAIN, I'LL ASK FOR PUBLIC COMMENT. THEN, MARIA, COULD YOU CALL THE ROLL? AND THE MOTION IS TO ACCEPT THE RECOMMENDATION AND APPROVE THIS FOR FUNDING.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.
DR. JUELSGAARD: YES.
MS. BONNEVILLE: KATHY LAPORTE.
MS. LAPORTE: YES.
MS. BONNEVILLE: LAUREN MILLER.
MS. MILLER: YES.
MS. BONNEVILLE: ADRIANA PADILLA.
DR. PADILLA: YES.
MS. BONNEVILLE: JOE PANETTA.
MR. PANETTA: YES.
MS. BONNEVILLE: FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: NO.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MS. BONNEVILLE: MOTION CARRIES.

MR. SHEEHY: GREAT. THANK YOU. SO DR. SAMBRANO, COULD WE NOW TAKE UP 08938?

DR. SAMBRANO: YES. THANK YOU, MR. SHEEHY. SO THIS NEXT APPLICATION IS FOR A PHASE III CLINICAL TRIAL OF AN ACELLULAR GRAFT FOR HEMODIALYSIS. SO THE THERAPEUTIC HERE IS AN IMPLANTED HUMAN ACELLULAR VESSEL, AND IT IS FOR END STAGE RENAL DISEASE PATIENTS THAT REQUIRE VASCULAR ACCESS FOR HEMODIALYSIS.

THE GOAL OF THIS WORK IS TO COMPLETE A PHASE III CLINICAL TRIAL TO GAIN FDA APPROVAL FOR CLINICAL USE OF THIS PRODUCT.

THE MAJOR PROPOSED ACTIVITIES INCLUDE THE MANUFACTURING AND DISTRIBUTION OF THIS ACELLULAR VESSEL FOR CLINICAL TESTING, ENROLLMENT OF PHASE III CLINICAL TRIAL, AND IMPLANTATION OF THE DEVICE INTO PATIENTS THAT REQUIRE VASCULAR ACCESS, AND THEN A LONGITUDINAL PATIENT FOLLOW-UP, DATA COLLECTION, AND ANALYSIS, AND ULTIMATELY REGULATORY APPROVAL FOR THE PRODUCT.

THE FUNDS REQUESTED ARE 9.9 MILLION, AND THERE IS AN EQUIVALENT AMOUNT OF CO-FUNDING THAT IS BEING PROVIDED.

THE NEXT SLIDE, WHICH IS THE OVERVIEW OF THE OUTCOME OF THE REVIEW. AGAIN, FOR THE BUDGET REVIEW THAT WE CONDUCT, THE APPLICATION PASSED. THE GRANTS WORKING GROUP REVIEWED THIS APPLICATION FOUR TIMES. IN THE FINAL REVIEW THE GRANTS WORKING GROUP GAVE THIS A SCORE OF 1. THERE WERE TEN VOTES GIVING IT A SCORE OF 1, ONE VOTE FOR A SCORE OF 2, AND THREE VOTES FOR A SCORE OF 3. THE CIRM TEAM AGREES AND CONCURS WITH THE RECOMMENDATION OF THE GRANTS WORKING GROUP TO AWARD 9.9 MILLION TO THIS APPLICANT. MR. SHEEHY.

MR. SHEEHY: SO COULD I GET A MOTION TO EITHER ACCEPT OR REJECT THE GRANTS WORKING GROUP RECOMMENDATION?

MS. WINOKUR: SECOND.

MR. SHEEHY: DO WE HAVE A MOTION MAKER? ARE YOU MAKING THE MOTION, DIANE?

MS. WINOKUR: YES.

MR. SHEEHY: AND IS THIS TO APPROVE? DO WE HAVE A MOTION TO APPROVE?

MR. ROWLETT: I'LL MOVE TO APPROVE.

MR. SHEEHY: AND THEN, DIANE, YOU'RE SECONDING, YES?

MS. WINOKUR: YES.

MR. SHEEHY: GREAT. GREAT. DO WE HAVE

DISCUSSION, QUESTIONS, COMMENTS?

DR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD AGAIN. SO TO BE QUITE HONEST AND I COULDN'T TELL FROM THIS PRESENTATION WHAT AN IMPLANTED HUMAN ACELLULAR VESSEL IS. AND SO I'D LIKE TO HAVE A LITTLE MORE DESCRIPTION OF EXACTLY WHAT IT IS WE'RE TALKING ABOUT.

AND THEN, AGAIN, I COULDN'T UNDERSTAND THE RELATIONSHIP BETWEEN WHATEVER THIS IS AND REGENERATIVE MEDICINE. SO IF SOMEBODY COULD SPEAK TO THE NEXUS BETWEEN WHATEVER IT IS THEY'RE TRYING TO DEVELOP HERE AND REGENERATIVE MEDICINE, THAT WOULD BE HELPFUL AS WELL.

WHEN I THINK OF VASCULAR ACCESS, I THINK OF THINGS LIKE PORTS. THESE ARE DEVICES THAT ARE INSERTED INTO THE BODY THAT ALLOW ACCESS IN THIS CASE TO A VEIN OR MIGHT IN THE CASE OF DELIVERING SOME DYE IF YOU ARE GOING TO DO PET SCANS OR WHATEVER WOULD BE INTO AN ARTERIAL VESSEL POTENTIALLY, WHATEVER. SO I'M JUST A LITTLE BIT LOST ABOUT WHAT THIS IS AND HOW THIS RELATES TO REGENERATIVE MEDICINE.

DR. SAMBRANO: SURE. THIS IS GIL. SO I'LL TRY TO PROVIDE YOU A BRIEF SUMMARY OF WHAT THIS IS. SO PATIENTS THAT UNDERGO HEMODIALYSIS OBVIOUSLY

NEED ACCESS TO THE VASCULATURE. AND AS YOU INDICATED, THERE ARE DIFFERENT WAYS IN WHICH THIS IS DONE. SO THERE ARE THINGS CALLED AND AV FISTULA WHERE THEY TAKE A PORTION OF VEIN FROM THE PATIENT AND THEY GRAFT IT IN ORDER TO ALLOW ACCESS OVER LONG PERIODS OF TIME TO THIS. SO THEY USE CATHETERS.

THIS IS A GRAFT THAT IS KIND OF DO TISSUE ENGINEERING GENERATED FROM AND IS COMPOSED OF EXTRACELLULAR MATRIX MATERIALS, COLLAGEN, FIBRONECTIN, VITRONECTIN, AND OTHER COMPONENTS. AND THROUGH THE CULTURE OF CELLS, IT GENERATES THIS GRAFT AS A LONG TUBE, AND THEN THAT IS DECELLULARIZED. ANY OF THE CELLS THAT WERE USED IN CREATING THAT GRAFT ARE REMOVED, AND SO THEN YOU HAVE WHAT IS THEN THE ACELLULAR GRAFT DEVICE THAT THEN IS USED IN PLACE OF WHAT WOULD BE AND AV FISTULA OR A CATHETER OR ANY OF THE OTHER TOOLS THAT ARE NORMALLY AVAILABLE.

AND WHEN IT'S IN PLACE IN THE PATIENT, THE GRAFT ITSELF RECRUITS STEM AND PROGENITOR CELLS THAT THEN POPULATE THE GRAFT ITSELF IN ORDER TO ALLOW THE GRAFT TO STAY IN PLACE. I HOPE THAT HELPS.

DR. JUELSGAARD: JUST QUICKLY, GIL, GO BACK TO THE REGENERATIVE MEDICINE ASPECT OF THIS. SO, AGAIN, WHERE DOES THAT FIT IN?

DR. SAMBRANO: WELL, IT IS GENERATING A HUMAN VESSEL. RIGHT? SO RATHER THAN HAVING TO TAKE A VEIN GRAFT FROM A PATIENT, YOU'RE GENERATING AN ARTIFICIAL VESSEL.

DR. JUELSGAARD: I REALIZE THAT. YOU SEE, THE WORD I GET HUNG UP ON HERE IS ACELLULAR. THAT MEANS WITHOUT CELLS, RIGHT. I NEVER CONSIDERED SOMETHING THAT WE WOULD FUND VIS-A-VIS REGENERATIVE MEDICINE -- WE FUND SMALL MOLECULES. LET ME AMEND THAT OR LARGE MOLECULES -- BUT ON THE DEVICE FRONT, SOMETHING THAT IS WITHOUT CELLS. SO THE THING THAT WE JUST TALKED ABOUT WITH DIABETES, RIGHT, IT'S CELLS THAT ARE CONTAINED WITHIN A MEMBRANE. I GOT THAT. THAT'S REGENERATIVE MEDICINE STUFF. I CAN UNDERSTAND THAT. I JUST AM HAVING A BIT MORE DIFFICULT TIME TRYING TO FIGURE OUT WHETHER THE REGENERATIVE MEDICINE ASPECT OF THIS IS THAT WE SHOULD BE FUNDING THIS WITH THE FUNDS THAT WE HAVE OR, AS I SAID, FOR REGENERATIVE MEDICINE PURPOSES.

DR. SAMBRANO: RIGHT.

DR. JUELSGAARD: I'M NOT SAYING THIS IS A BAD IDEA. I'M JUST NOT SURE THIS IS WITHIN OUR MANDATE.

DR. SAMBRANO: RIGHT. ONE, WE DO EVALUATE APPLICATIONS FOR ELIGIBILITY. AND CERTAINLY WE WANT

TO MAKE SURE, AS WELL AS YOU, THAT THESE ARE PROGRAMS THAT ARE GOING TO BE ELIGIBLE. THE REGENERATIVE PART THAT YOU'RE ASKING ABOUT COMES INTO PLAY WHEN THE GRAFT IS PLACED ON THE PATIENT AND THE CELLS FROM THE PATIENT THEN ALLOW -- INFILTRATE THE GRAFT, THEY POPULATE IT, AND ALLOW THIS GRAFT TO STAY IN PLACE IN ORDER TO SERVE AS A CONDUIT FOR THE VASCULATURE AND FOR ACCESS INTO THE VASCULATURE. SO IT IS ANALOGOUS TO A TRANSPLANT OF ANY OTHER VESSEL FOR A MULTITUDE OF PURPOSES. IN THIS CASE IT IS FOR THE PURPOSE OF HEMODIALYSIS.

DR. JUELSGAARD: LET ME JUST FOLLOW UP ON THAT. SO LET'S ASSUME SOMEBODY COMES UP WITH A NEW METHODOLOGY FOR SKIN GRAFTING OR FOR KIDNEY TRANSPLANT OR ANY OTHER THING WHERE NEW CELLS ARE GOING TO HAVE TO BE DEVELOPED. THE BODY WILL DEVELOP NEW CELLS IN ORDER TO ACCEPT THAT SKIN GRAFT OR TO ACCEPT THAT KIDNEY TRANSPLANT, ETC. IS ALL OF THAT WITHIN OUR AMBIT OF WHAT ARE MISSION IS ABOUT?

DR. SAMBRANO: YES. AS LONG AS IT INVOLVES STEM OR PROGENITOR CELLS AS AN ASPECT OF IT, THEN, YES, IT DOES.

DR. JUELSGAARD: AND HOW DO YOU KNOW THAT THIS INVOLVES A STEM OR PROGENITOR CELL? HOW DO WE KNOW THAT THEY'RE INVOLVED AT ALL? ARE WE TO ASSUME

THAT THAT'S THE CASE?

DR. SAMBRANO: NO. THIS IS SOMETHING THAT WHEN THE APPLICANTS APPLIED, IT WAS ONE OF OUR FIRST QUESTIONS IN TERMS OF PROVIDING EVIDENCE THAT THIS HAPPENS. AND SO THEY HAVE DATA AND HAVE DONE HISTOLOGY OF THE GRAFTS AFTER IMPLANTATION THAT SHOWS THAT STEM/PROGENITOR CELLS ARE INVOLVED IN BEING -- THAT THEY ARE RECRUITED TO THE GRAFT, THEY ENTER THE GRAFT, AND ARE RESPONSIBLE FOR MEDIATING THE CELL POPULATION THAT ULTIMATELY MAKES THE GRAFT WORK.

DR. PRIETO: GIL, CAN I RESPOND TO THAT AND MAKE SOME COMMENTS?

DR. SAMBRANO: YES.

DR. PRIETO: SO THIS IS FRANCISCO, AND I WAS ONE OF THE REVIEWERS ON THIS GRANT, I GUESS, AT LEAST A COUPLE OF TIMES. AND I HAD SEVERAL CONCERNS ABOUT THIS, AND SO I WANT TO EXPLAIN WHY, ALTHOUGH I VOTED TO MOVE IT ALONG TO THE FULL BOARD, TO THE ICOC, I'M GOING TO VOTE AGAINST IT. AND SOME OF THE CONCERNS HAVE TO DO WITH WHAT STEVE BROUGHT UP. I QUESTIONED HOW REGENERATIVE THIS WAS. THEY DO USE CELLS TO GROW THE TUBE THAT THEY ARE GOING TO THEN DECELLULARIZE AND ENGRAFT. OF COURSE, THAT TUBE WILL THEN BE REPOPULATED WITH THE CELLS. BUT

ESSENTIALLY THAT SEEMED A LITTLE BIT MARGINAL TO ME.

THE GROUP, IT SEEMS TO ME, IS HIGHLY COMPETENT, MORE THAN CAPABLE OF DOING THE WORK THAT THEY SAY THEY WANT TO DO. THEY CAME BACK EACH TIME WE SUGGESTED THAT THIS OR THAT SHOULD BE TWEAKED, WE GAVE THIS A 2, I BELIEVE, AT LEAST TWICE. THEY ANSWERED THOSE CONCERNS AND CAME BACK. SO I BELIEVE THEY'RE CAPABLE OF DOING THE WORK.

I ALSO THINK, PARTICULARLY CONSIDERING HOW MARGINALLY REGENERATIVE THIS IS, THAT THIS IS LIKELY A GRANT THAT CAN BE FUNDED ELSEWHERE THAT WOULD QUALIFY UNDER VARIOUS OTHER FUNDING AGENCY'S GUIDELINES AND WOULD BE PROMISING ENOUGH THAT THEY'RE LIKELY TO FIND FUNDING SOMEWHERE.

THE OTHER QUESTION AND REALLY MAIN CONCERN WAS WHETHER THIS IS TRULY ADDRESSING AN UNMET NEED. TO MY MIND THIS IS ADDRESSING WITH A MARGINAL IMPROVEMENT AN IMPERFECTLY MET NEED. AS GIL SAID, THERE ARE SEVERAL WAYS THAT HEMODIALYSIS CAN BE PROVIDED TO A PERSON NOW. ONE OF THEM IS THE AV FISTULA IN WHICH AN ARTERY IS CONNECTED DIRECTLY TO A NATIVE VEIN, SO THE VEIN DILATES AND YOU CAN INSERT A NEEDLE, A CATHETER, INTO THAT AND DIALIZE THREE TIMES A WEEK.

YOU CAN INSERT A CATHETER, A SYNTHETIC

CATHETER, INTO A LARGE VEIN SUCH AS THE SUBCLAVIAN VEIN AND USE THAT TEMPORARILY. IN FACT, THAT'S COMMONLY DONE WHILE PEOPLE ARE HAVING A FISTULA MATURE AFTER THEIR SURGERY. THERE ARE SYNTHETIC GRAFTS. I BELIEVE GORTEX IS THE MATERIAL THAT'S USED. AND THOSE ARE PUT INTO CREATE FISTULAS WHICH CAN THEN BE ACCESSED ROUTINELY FOR DIALYSIS.

SO THERE ARE VARIOUS WAYS, AND IT'S RARE IN MY EXPERIENCE AS A CLINICIAN, I'D HAVE TO SAY I HAVE NOT SEEN IT, FOR A PATIENT TO BE UNABLE TO BE DIALIZED. EACH ONE OF THESE APPROACHES HAVE THEIR ADVANTAGES AND DISADVANTAGES, AND THERE'S MORE OR LESS RISK OF INFECTION AND VARIOUS COMPLICATIONS, AND THERE'S MORBIDITY AND MORTALITY ATTACHED TO ALL OF THAT AS THERE IS TO KIDNEY FAILURE ITSELF, BUT THIS SEEMS TO ME A VERY MARGINAL IMPROVEMENT ON AN EXISTING IMPERFECTLY MET NEED BY USING AN APPROACH THAT IS NOT ALL THAT REGENERATIVE. AND SO I'M GOING TO VOTE, SUGGEST THEY GO ELSEWHERE.

DR. DULIEGE: JUST TO RESPOND TO THE COMMENT THAT WAS JUST MADE, I'D LOVE TO HEAR BACK FROM THE CIRM TEAM IN THE SENSE OF REGENERATIVE MEDICINE, BUT I THOUGHT THAT OUR ROLE AS MEMBER OF THE ICOC IS NOT SO MUCH TO CHALLENGE WHETHER THIS SHOULD HAVE BEEN FILED AS AN APPLICATION FOR FUNDING

IN THE FIRST PLACE, BUT TO REVIEW THE MERIT OF THE REVIEW PROCESS AND ENSURE THAT WE ARE IN AGREEMENT OR POTENTIALLY IN AGREEMENT WITH IT.

WHAT I'M TRYING TO SAY IS IF TRULY CIRM FELT THAT THIS IS NOT WITHIN THE SCOPE OF CERTAIN (INAUDIBLE) WHICH HAVE SAID THAT TO THE APPLICANTS TO BEGIN WITH, BUT NOT WAIT FOR THEM TO GO THROUGH THE ENTIRE APPLICATION REVIEW PROCESS TO SAY, OH, AND BY THE WAY, IT'S NOT WITHIN THE SCOPE OF WHAT WE WOULD LIKE TO FUND, IF I UNDERSTOOD THE PREVIOUS COMMENT. SO MAYBE THE CIRM STAFF SHOULD RESPOND TO THAT, WHICH IS SHOULD IT BE WITHIN THE SCOPE OF WHAT WE SHOULD BE FUNDING IF WE BELIEVE THAT THE APPLICATION IS (INAUDIBLE).

CHAIRMAN THOMAS: JEFF, RANDY WOULD LIKE TO COMMENT AND RESPOND TO ANNE-MARIE'S QUESTION.

DR. MILLS: WITH REGARDS TO SCOPE, THE SCOPE -- SO THIS APPLICATION CLEARLY FELL WITHIN THE STATED SCOPE OF THE CONCEPT PLAN THAT WAS OPEN, THAT IS OPEN NOW. AND THAT SCOPE WAS SOMETHING THAT WAS REVIEWED AND APPROVED BY THIS BOARD. AND SO THE APPROPRIATE VENUE TO DISCUSS AND MODIFY SCOPE IS AROUND MODIFYING THE CONCEPT PLAN REALLY. IF THAT'S SOMETHING WE WANT TO TAKE UP, WE SHOULD DO, BUT RIGHT NOW AND FOR A LONG TIME THE SCOPE IS SUCH THAT

WE ALLOW THINGS THAT USE STEM CELLS IN THE MANUFACTURING OF THE PRODUCT OR THE STEM CELL ITSELF OR ACTS UPON A STEM CELL WHEN PLACED IN. SO IF THAT'S SOMETHING WE WANT TO ADDRESS, WE SHOULD DO AT THE RIGHT TIME. BUT I JUST WANT TO MAKE CLEAR THAT THIS BOARD REVIEWED, THE ENTIRE BOARD, REVIEWED AND APPROVED THE CONCEPT PLAN WHICH INCLUDED THE SCOPE PREVIOUSLY.

DR. JUELSGAARD: SO THIS IS STEVE JUELSGAARD. CAN I JUST RESPOND TO BOTH WHAT ANNE-MARIE AND RANDY JUST SAID? SO I'M GOING TO -- THERE ARE THREE THINGS THAT ARE IMPORTANT TO ME. I'M GOING TO AGREE WITH FRANCISCO. I'M GOING TO VOTE AGAINST IT JUST SO YOU KNOW UP FRONT.

SO THE FIRST THING IS WE'RE TALKING ABOUT $10 MILLION HERE. AND WE'RE GETTING DOWN TO THE LAST DOLLARS AS TIME ROLLS ON. AND I THINK IT'S CRITICAL THAT WE REALLY TAKE A LOOK AT WHAT WE'RE FUNDING AND BELIEVE THAT THIS IS IMPORTANT FOR US TO FUND AND THERE TRULY IS, AS PROP 71 SAID, NO OTHER AVENUE OF FUNDING, WHICH WAS ONE OF THE THINGS THAT WAS SPECIFIED AT THE BEGINNING. I'M A LITTLE WORRIED THAT THEY PROBABLY ARE HERE, BUT WE HAPPEN TO BE A WATERING TROUGH TO SOLVE THAT.

THE SECOND THING IS THE THINGS THAT

FRANCISCO SAID. ANNE-MARIE, THE THINGS THAT THIS COMMITTEE IS SUPPOSED TO ENGAGE IN, AT LEAST MY UNDERSTANDING, IS PROGRAMMATIC REVIEW WITHOUT INVOLVING SCIENTIFIC REVIEW. AND WE'RE NOT TALKING ABOUT THAT. WE'RE TALKING ABOUT WHETHER THIS REALLY FITS WITH OUR PROGRAM. AND I BELIEVE THAT'S REALLY OUR RESPONSIBILITY, AND IT'S WHOLLY UNCLEAR TO ME HOW WELL THIS REALLY FITS WITH OUR PROGRAM.

IT'S NICE TO SAY THAT THIS IS PART OF THE CONCEPT, BUT THIS IS WHERE THE RUBBER MEETS THE ROAD. THIS IS OUR JOB. WE NEED TO FIGURE OUT WHETHER WE BELIEVE THIS IS WORTH FUNDING OR NOT. FORGET ABOUT THE CONCEPT. THIS IS -- WE'RE THE ONES WHO DECIDE HOW THE MONEY GETS SPENT, AND WE NEED TO BE COMFORTABLE THAT WE'RE MAKING A GOOD DECISION.

AND THE THIRD THING IS I'M SORRY THAT SOMEBODY CAME BACK FOUR TIMES TO COME UP WITH A PERFECT APPLICATION, BUT THAT DOESN'T CHANGE MY POINT OF VIEW. I DON'T WANT TO DO THIS BECAUSE I FEEL SORRY FOR SOMEBODY. I WANT TO GIVE THEM MONEY BECAUSE I FEEL THAT THEY DESERVE IT BECAUSE THEY'RE DOING WHAT IT IS THAT WE'RE COMMISSIONED TO HAVE THEM DO, AND THAT IS TO ADVANCE THE FIELD OF REGENERATIVE MEDICINE, WHICH IS NOT AT ALL CLEAR TO ME HERE.

SO FOR THOSE REASONS I WILL VOTE AGAINST THIS, AND I WILL KEEP MY MOUTH SHUT FROM HERE ON.

DR. MILLS: STEVE, I CAN APPRECIATE THAT, AND I WOULDN'T SUGGEST NOT VOTING WHAT YOU THINK IS RIGHT. THE ONLY THING -- THE POINT I WAS TRYING TO MAKE AND PROBABLY DIDN'T ARTICULATE VERY WELL IS THAT IF WE DON'T LIKE THE CONCEPT, WE DON'T LIKE THE SCOPE OF THE CURRENT CONCEPT PLAN, IT'S VERY, VERY IMPORTANT THAT WE BRING THAT BACK UP AND WE AMEND IT TO THE WAY WE WANT IT TO BE BECAUSE JUST OPERATIONALLY IT'S A VERY DIFFICULT THING FOR US AS AN ORGANIZATION TO GO OUT AND TRY TO RECRUIT PROMISING PROGRAMS SAYING THIS IS THE SCOPE -- THIS IS THE SCOPE OF THE THING THAT CIRM WANTS AND THEN LATER SAY, WE KNOW WE SAID THAT'S WHAT WE WANTED, BUT IT'S NOT WHAT WE WANTED.

SO I GUESS WHAT I'M SAYING IS THIS EASILY FALLS WITHIN THE FOUR CORNERS OF THE CURRENT STATED SCOPE. AND IF THAT'S NOT WHAT WE WANT, I WOULD JUST ASK THAT WE JUST ADDRESS IT SO WE HAVE MORE CLEAR DIRECTION ON WHAT IT IS WE DO WANT.

CHAIRMAN THOMAS: STEVE, THIS IS J.T. A COUPLE POINTS. NO. 1, HAVING SAT THROUGH THE GRANTS WORKING GROUP WITH RESPECT TO THIS PROPOSAL OR ANY PROPOSAL, EVEN THOUGH IT WAS IDENTIFIED GOING IN AS

BEING WITHIN SCOPE, IT'S FREQUENTLY THE CASE AT THE GRANTS WORKING GROUP THAT IF MEMBERS OF THAT GROUP FEEL THAT FOR SOME REASON IT IS TOO MARGINAL OR DOESN'T HAVE A SUFFICIENT REGENERATIVE ELEMENT, THEY'LL BRING THAT UP AND THERE WILL BE A ROBUST DISCUSSION ON THE TOPIC.

AT THIS PARTICULAR REVIEW, AT THE END OF THE DAY, THAT ASPECT OF THIS WAS NOT SOMETHING THAT CAUSED THE VOTING MEMBERS OF THE GRANTS WORKING GROUP TO OPPOSE THIS. IN FACT, THEY DECIDED TO GO AHEAD WITH A FAIRLY LARGE MAJORITY APPROVE IT AS A FUNDABLE PROJECT. SO THAT'S THE FIRST POINT.

THE SECOND POINT IS WITH RESPECT TO ALTERNATIVE SOURCES OF FUNDING, WE ARE ABOUT TRYING TO HELP LEVERAGE OUR MONEY AGAINST OTHER SOURCES AND, IN FACT, HOPE THAT WHEN WE DO FUND SOMETHING, INDEED, THERE ARE OTHER SOURCES OF MONEY THAT WILL COME IN ON TOP OF OUR FUNDING TO FURTHER WHATEVER THE PROJECT AT ISSUE MAY HAPPEN TO BE. SO THE FACT THAT THERE MAY BE OTHER SOURCES AVAILABLE, TO ME AT LEAST, IF THIS IS SOMETHING THAT DOES COME WITHIN OUR SCOPE AND WAS RECOMMENDED BY THE BOARD -- I'M SORRY -- BY THE GRANTS WORKING GROUP AND WAS NOT SEEN TO BE SO MARGINAL AS TO PUT IT OUT OF CONTENTION, I'M OKAY WITH THAT.

DR. PRIETO: FRANCISCO AGAIN. I JUST WOULD LIKE TO SAY THAT, AGAIN, I VOTED TO BRING THIS TO THE ICOC. ALTHOUGH I MENTIONED OTHER POINTS, IT WAS BECAUSE I THOUGHT THAT THIS WAS A VERY SCIENTIFICALLY CAPABLE GROUP, BUT I THOUGHT THAT MY PRINCIPAL OBJECTIONS WERE PROGRAMMATIC. AND THAT WAS SOMETHING -- THAT'S SOMETHING THAT HAS TO BE DECIDED BY THE BOARD, NOT AT THE GWG. SO HERE WE ARE.

MR. SHEEHY: YEAH. AND, FRANCISCO, COULD YOU JUST RESTATE? I THINK YOU HAD TWO POINTS THAT YOU WERE MAKING PROGRAMMATICALLY.

DR. PRIETO: WELL, THE MAIN CONCERN IN MY MIND WAS THAT THIS IS NOT SO MUCH AN UNMET NEED AS AN IMPERFECTLY MET NEED, AND THAT I THOUGHT THIS WILL BE A MARGINAL IMPROVEMENT, BUT IT'S NOT A DISEASE OR CONDITION THAT IS CURRENTLY UNTREATED OR FOR WHICH THERE IS NO ALTERNATIVE OPTION, AS WOULD BE THE CASE IF WE WERE DEALING WITH -- WELL, I DON'T KNOW IF I WANT TO BRING IN OTHER DISEASES. BUT IT DIDN'T SEEM TO ME TO BE AN UNMET NEED. I THINK THAT'S MY PRIMARY CONCERN.

MR. SHEEHY: THANK YOU. SO GREAT DISCUSSION. DO WE HAVE MORE QUESTIONS OR COMMENTS FROM MEMBERS OF THE COMMITTEE? DO WE HAVE ANY

PUBLIC COMMENT AT ANY OF THE SITES?

DR. SAMBRANO: WE DO IN OAKLAND.

DR. BOTKIN: CAN YOU HEAR ME ON THE PHONE? THIS IS JEFF BOTKIN. I'M ACTUALLY THE CHIEF MEDICAL OFFICER OF HUMACYTE AND A PROFESSOR OF SURGERY AND PATHOLOGY AT DUKE UNIVERSITY, AND I FLEW OUT HERE JUST TO BE PRESENT TO PARTICIPATE IN THIS DISCUSSION. AND I APPRECIATE ALL THE COMMENTS.

FIRST, IN THE REGENERATIVE MEDICINE QUESTION, WE ARE THE FIRST TISSUE-ENGINEERED STRUCTURE, IN THIS CASE A TISSUE-ENGINEERED BLOOD VESSEL, TO ENTER PHASE III CLINICAL TESTING IN HUMAN IMPLANTS. WE THINK WE'RE THE VERY SIMPLEST ORGAN IN THIS REGENERATIVE MEDICINE SPACE OUT OF A BLOOD VESSEL, BUT IT'S A SIMPLE ORGAN, BUT IT MEETS ALL OF THE CRITERIA FOR MAKING MORE COMPLEX ORGANS.

IN THIS CASE WE MAKE A STRUCTURE FROM CELLS MADE INITIALLY FROM HUMAN AORTIC VASCULAR SMOOTH MUSCLE CELLS AND WE CREATE THIS TUBE. IN THIS CASE IT'S 40 CENTIMETERS LONG, 6 MILLIMETERS IN DIAMETER, AND THEN IS DECELLULARIZED TO REMOVE ALL OF THE ANTIGENS FROM THE ORIGINAL DONOR SO WE CAN IMPLANT IT INTO ANYONE. BUT TO MAKE IT A LIVING TISSUE, IT'S REQUIRED TO BE REPOPULATED WITH STEM CELLS. IN THIS CASE A MYELOID PROGENITOR CELL GOES

INTO WHAT IS THE FUNCTIONAL MEDIA OF THE VESSEL AND REPOPULATES IT WITH SOMETHING THAT HISTOLOGICALLY LOOKS LIKE THE VASCULAR SMOOTH MUSCLE CELL. AND ENDOTHELIAL PROGENITOR CELLS LAND ON THE SURFACE OF THIS AND RELINE IT AND COMPLETELY RE-ENDOTHELIALIZE THE TUBE SO THAT THE STRUCTURE THAT WE'VE IMPLANTED IS HISTOLOGICALLY IDENTICAL TO A BLOOD VESSEL FROM THE HOST.

AND WE BELIEVE THAT THAT'S THE FUNDAMENTAL PLATFORM THAT OTHER REPOPULATION OF MORE COMPLEX ORGANS WILL BE DERIVED FROM. SO THIS IS VERY MUCH IN THE WHEELHOUSE OF REGENERATIVE MEDICINE. WE JUST PROVIDE A STRUCTURE THAT THE HOST REPOPULATES AND REMODELS. WE HAVE A SIGNIFICANT AMOUNT OF SCIENCE WE HAVE GOING FORWARD.

WITH RESPECT TO THE UNMET CLINICAL NEED, WE'RE MAKING A BLOOD VESSEL. THE BLOOD VESSEL'S ENTRY POINTS IN THIS CASE BY THE FDA IS IN DIALYSIS ACCESS. THAT'S BECAUSE IT'S THE SAFEST PLACE TO OBSERVE THE BLOOD VESSEL. WE HAVE EVERY INTENTION AND, IN FACT, CLINICAL DEVELOPMENT PROGRAMS, PHASE II PROGRAMS, ALREADY FOR LOWER EXTREMITY ARTERIAL RECONSTRUCTION, AND WE'VE ALREADY DONE PRECLINICAL WORK IN THE OTHER BLOOD VESSEL SPACES OF CORONARY ARTERY BYPASS SURGERY.

THE VASCULAR ACCESS SPACE, JUST TO RESPOND TO THAT, IS A VERY COMPLEX CLINICAL AREA. AND AS NOTED, THERE ARE OTHER DEVICE OR TECHNOLOGIES AVAILABLE, BUT LET'S TALK ABOUT EACH ONE FOR ONE SECOND.

DIALYSIS CATHETERS, WHICH CAN BE PLACED IN PEOPLE EASILY, HAVE AN INFECTION RATE OF ABOUT EVERY THREE TO SIX MONTHS THEY FAIL AND HAVE TO BE REPLACED, WHICH ARE BOTH EXPENSIVE AND CAUSE THINGS LIKE SEPTICEMIA. VASCULAR SYNTHETIC GRAFTS MADE OF TEFLON OR GORTEX FAIL PREDICTABLY ABOUT ONCE A YEAR, WHICH, AGAIN, CAUSES A SIGNIFICANT AMOUNT OF MORBIDITY AND HEALTHCARE EXPENSE FOR THOSE PATIENTS. AND THE PATIENTS WITH THE INTENT TO USE THEIR OWN VEIN, CALLED AND AV FISTULA, HAS A 50 PERCENT FAILURE OF MATURATION. SO EACH ONE OF THOSE CLINICAL AREAS STILL HAS SIGNIFICANT MORBIDITY AND ASSOCIATED MORTALITY.

WE PUT THIS CASE BEFORE THE FDA, AND THEY FELT SO COMPELLED THAT THIS IS A SOLUTION THAT THEY GAVE US FAST-TRACK DESIGNATION FOR THIS UNMET CLINICAL NEED IN AND OF ITSELF INDEPENDENT OF ALL OF THE OTHER AREAS WHICH WE WILL TOUCH AS WE GO THROUGH OUR CLINICAL APPROVAL PROCESS IN VASCULAR ACCESS, ARTERIAL RECONSTRUCTION, AND CORONARY ARTERY

RECONSTRUCTION AS WE MOVE FORWARD. SO WE THINK THAT THERE'S A SIGNIFICANT UNMET CLINICAL NEED IN THE DIALYSIS SPACE ITSELF AND A HUGE UNMET CLINICAL NEED IN VASCULAR RECONSTRUCTION FOR EVERYONE, LET IT BE AN ELDERLY PATIENT WITH LOWER EXTREMITY ARTERIAL DISEASE OR AN INJURED WARRIOR WHERE THERE IS NO CONDUIT AVAILABLE AFTER THEY'VE HAD A BLAST INJURY FROM AN IED AND THE FORWARD OPERATING FACILITIES HAVE NO OFF-THE-SHELF VASCULAR CONDUIT AVAILABLE TO RECONSTRUCT THEIR LEGS.

SO WITH THAT, I WILL STOP AND HOPEFULLY ANSWER THOSE QUESTIONS.

MR. SHEEHY: THANK YOU, DR. BOTKIN. DO WE HAVE ANY OTHER PUBLIC COMMENT?

DR. JUELSGAARD: JEFF, THIS IS NOT THE PUBLIC, THIS IS STEVE. BUT LET ME JUST ASK DR. BOTKIN FOR A MOMENT. SO YOU SAY YOU HAVE FAST-TRACK DESIGNATION BY THE FDA. SO IS THIS A CASE THAT YOU'RE SIMPLY ONLY GOING TO BE HELD TO ONE PHASE III CLINICAL TRIAL FOR APPROVAL WITH A FOLLOW-UP PHASE III CLINICAL TRIAL, OR WHAT EXACTLY DO YOU NEED?

DR. BOTKIN: CURRENTLY BY OUR SPA APPROVAL, SO WE HAVE A FAST-TRACK DESIGNATION AND A SPECIAL PROTOCOL AGREEMENT WITH THE FDA, WE ONLY ARE REQUIRED TO HAVE ONE PIVOTAL CLINICAL TRIAL FOR

VASCULAR ACCESS APPROVAL. WE WILL BE REQUIRED TO HAVE AN ADDITIONAL PIVOTAL CLINICAL TRIAL FOR LOWER EXTREMITY ARTERIAL RECONSTRUCTION; BUT FOR DIALYSIS ACCESS, WE'RE CURRENTLY ONLY REQUIRED TO HAVE ONE FOR APPROVAL.

DR. JUELSGAARD: AND SO THERE IS NO POSTMARKETING, THEN, FOLLOW-UP ON THIS FIRST PHASE III CLINICAL TRIAL THAT'S GOING TO BE REQUIRED BY THE FDA BECAUSE NORMALLY, AT LEAST IN MY EXPERIENCE, YOU CAN SUBMIT ON ONE PHASE III CLINICAL TRIAL, BUT THEN THEY WANT TO SEE A FOLLOW-UP TO VALIDATE THAT, INDEED, WHAT YOU SAW ON THE FIRST PHASE III IF SUCCESSFUL IN A SECOND SIMILAR TRIAL.

DR. BOTKIN: THAT IS CURRENTLY NOT THE CASE WITH OUR DISCUSSION WITH THE FDA AND OUR APPROVED SPA.

DR. JUELSGAARD: ALL RIGHT. THANK YOU.

MR. SHEEHY: ADDITIONAL QUESTIONS OR COMMENTS? OKAY. I THINK NO PUBLIC COMMENTS, NO ADDITIONAL COMMENTS FROM THE BOARD, THEN I THINK WE'RE READY TO CALL THE ROLL. MARIA, PLEASE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: I'LL CHANGE MY VOTE TO A YES.

MS. BONNEVILLE: LAUREN MILLER.

MS. MILLER: YES.

MS. BONNEVILLE: ADRIANA PADILLA.

DR. PADILLA: YES.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: YES.

MS. BONNEVILLE: FRANCISCO PRIETO. ROBERT QUINT.

DR. QUINT: NO.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: YES.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

DR. STEWARD: I'M HERE AND I'M A YES. THIS IS OS.

MR. HARRISON: OS, YOU'RE CONFLICTED ON

THIS ONE.

DR. STEWARD: OKAY. SORRY ABOUT THAT. I'M HERE THEN AND I DO NOT VOTE.

MS. LAPORTE: THIS IS KATHY AND I'M A YES AS WELL.

MS. BONNEVILLE: KATHY, YOU'RE ALSO CONFLICTED.

MS. LAPORTE: OH, GOOD TO KNOW.

MR. SHEEHY: SO THE STATUS OF THE MOTION?

MS. BONNEVILLE: MOTION CARRIES.

MR. SHEEHY: GREAT. THANK YOU. AND THANK YOU, DR. BOTKIN. CONGRATULATIONS.

OKAY. NEXT, I THINK, ON THE AGENDA IS THE QUEST AWARDS, AND SO WILL YOU TAKE US THROUGH THIS, DR. SAMBRANO?

DR. SAMBRANO: YES, I WILL. SO THERE IS A SECOND SET OF SLIDES FOR THE QUEST PROGRAM AND THE CHALLENGE PROGRAMS, AND WE'LL GO THROUGH THE QUEST PROGRAM FIRST.

SO I HAVE A SLIDE THAT SHOWS WHERE OUR DISCOVERY PROGRAM FITS ALONG THE DEVELOPMENT PIPELINE. AND SO THIS OBVIOUSLY FALLS INTO THE DISCOVERY INITIATIVES THAT WE OFFER TWO TIMES A YEAR IN ORDER TO PROMOTE PRODUCTS THAT WILL GO INTO THE TRANSLATIONAL PROGRAMS DOWN THE LINE.

THE OBJECTIVE OF THE QUEST PROGRAM IS TO PROMOTE THE DISCOVERY OF PROMISING NEW STEM CELL-BASED TECHNOLOGIES THAT COULD BE TRANSLATED TO ENABLE THEIR BROAD USE AND ULTIMATELY TO IMPROVE PATIENT CARE. SO PROJECTS THAT WOULD BE CONSIDERED UNDER THIS PROGRAM INCLUDE THOSE THAT ARE UNIQUELY ENABLED BY HUMAN STEM/PROGENITOR CELLS OR DIRECTLY REPROGRAMMED CELLS OR THAT ARE UNIQUELY ENABLING FOR THE ADVANCEMENT OF STEM CELL-BASED THERAPIES.

SOME OF THE KEY POINTS IN INSTRUCTING REVIEWERS IN TERMS OF WHAT WE WERE LOOKING FOR, WE LOOKED FOR PROJECTS THAT HAVE THE CAPABILITY TO DEVELOP A NOVEL CANDIDATE PRODUCT. SO IT CAN BE ANY OF THE FOLLOWING: A THERAPEUTIC, A DIAGNOSTIC, A MEDICAL DEVICE, OR A TOOL THAT WOULD BE READY FOR TRANSLATIONAL STUDIES WITHIN TWO YEARS.

THE PRODUCT TYPE, OF COURSE, BECAUSE OF THEIR NATURE, DETERMINE THE SPECIFIC OUTCOMES THAT ARE EXPECTED AND, THEREFORE, THE READINESS FOR THOSE TRANSLATIONAL STUDIES. SO THAT IS PART OF THE CONSIDERATION OF THE GROUP.

AND IF SUCCESSFULLY REALIZED THAT THE CANDIDATE OFFERS THE POTENTIAL TO IMPROVE PATIENT CARE OR THAT IT FACILITATES THE DISCOVERY, DEVELOPMENT, OR USE OF STEM CELL-BASED THERAPIES.

THE REVIEW CRITERIA ARE THE FOUR THAT WE NORMALLY USE ACROSS OUR INITIATIVES. DOES THE PROJECT HOLD THE NECESSARY SIGNIFICANCE AND POTENTIAL FOR IMPACT? IN THIS CASE IS THIS A PROJECT THAT IS LIKELY WITHIN A TWO-YEAR TIME SPAN TO DELIVER A PRODUCT THAT IS READY FOR TRANSLATIONAL WORK AND ONE THAT IS GOING TO ADVANCE STEM CELL-BASED THERAPIES IN SOME WAY?

IS THE RATIONALE SOUND, MEANING DOES THIS MAKE SENSE?

IS THE PROJECT WELL-PLANNED AND DESIGNED?

AND IS IT FEASIBLE; THAT IS, IS IT SOMETHING THAT THE GROUP CAN DO AND ACCOMPLISH?

OKAY. SO I WILL GO INTO THE RECOMMENDATIONS FROM THE GRANTS WORKING GROUP, BUT I WILL REMIND YOU HERE THAT THE SCORING SYSTEM IS DIFFERENT FOR OUR DISCOVERY TRANSLATION PROGRAMS. SO FOR QUEST, REVIEWERS USE A SCORE OF 1 TO 100 WITH 100 BEING THE BEST POSSIBLE SCORE IN WHICH THEY CAN PLACE THE APPLICATION. SO A SCORE OF 85 TO 100 MEANS THAT THEY RECOMMEND FUNDING IF FUNDS ARE AVAILABLE. AND IF THEY SCORE IT 1 THROUGH 84, IT MEANS THAT THEY ARE NOT RECOMMENDING FUNDING. AND APPLICATIONS ARE SCORED BY ALL THE SCIENTIFIC MEMBERS OF THE GWG THAT DO NOT HAVE A CONFLICT.

SO IN THIS NEXT SLIDE I'M SHOWING A TABLE OF THE 43 APPLICATIONS THAT WERE REVIEWED BY THE GWG. FOLLOWING THE REVIEW, THERE WERE FIVE THAT SCORED IN THE RECOMMENDED FOR FUNDING RANGE, AND THERE WERE 38 THAT FELL INTO THE NOT RECOMMENDED FOR FUNDING. AS ALWAYS, AT THE END OF THE REVIEW, WE HAVE THE GRANTS WORKING GROUP TAKE A VOTE ON THE REVIEW PROCESS OVERALL. IN PARTICULAR, TO NOTE THAT THE ICOC PATIENT ADVOCATE MEMBERS TAKE A VOTE ON WHETHER THE REVIEW WAS CARRIED OUT IN A FAIR MANNER AND WAS FREE FROM UNDUE BIAS. SO THESE VOTES -- THE MEMBERS VOTED UNANIMOUSLY IN FAVOR OF THE FAIR PROCESS.

SO I'LL TAKE YOU, THEN, TO THE LAST SLIDE FOR THE QUEST PROGRAM WHICH PRESENTS CIRM TEAM RECOMMENDATIONS, AND YOU WILL NOTICE THAT WE ARE RECOMMENDING A TOTAL OF SEVEN APPLICATIONS FOR FUNDING, WHICH INCLUDES THE FIVE THAT ARE RECOMMENDED BY THE GWG BASED ON THE SCORE AS WELL AS TWO ADDITIONAL ONES, WHICH IF YOU LOOK AT THE TABLE BELOW, INCLUDE APPLICATIONS 9073 AND 8982. THEY RECEIVED A SCORE OF 83 AND 81 RESPECTIVELY. THEIR MEDIAN IN BOTH CASES WAS AN 85, AND ALSO IN BOTH CASES, IF YOU LOOK AT THE NUMBER OF MEMBERS SCORING WITHIN EACH CATEGORY, OVER TWO-THIRDS OF THE MEMBERS

SCORED THESE APPLICATIONS IN THE RECOMMENDED FOR FUNDING CATEGORY, TEN AS OPPOSED TO FOUR.

SO WE FELT THAT IN THIS CASE THE WAY THE SCORING SYSTEM WORKS THAT UTILIZES THE MEAN DID NOT REALLY REFLECT THE VOTE OR THE INTENT OF THE GRANTS WORKING GROUP IF YOU LOOK AT HOW THEY SCORE, THE TEN TO FOUR VOTE PLACING IT IN THE FUNDABLE CATEGORY.

SO THAT IF SEVEN APPLICATIONS WERE TO BE FUNDED, THAT WOULD TAKE US TO 13.6 MILLION TOTAL FOR THIS PROGRAM. SO HAPPY TO TAKE ANY QUESTIONS.

MR. SHEEHY: ONE QUICK QUESTION, GIL. WHAT'S THE BUDGET FOR THIS ROUND?

DR. SAMBRANO: SO PAT TELLS ME 17.5 IS WHAT WE HAVE AVAILABLE FOR THIS ROUND.

MR. SHEEHY: GREAT. GREAT. SO I THINK MAYBE THE BEST WAY TO PROCEED IS THE WAY WE USUALLY DO THIS, WHICH IS TO SEE IF THERE ARE ANY, BECAUSE THERE'S SO MANY APPLICATIONS, IS TO SEE IF THERE'S A MOTION TO MOVE ANY APPLICATION OUT OF TIER I. AND THEN I THINK EACH OF THE CIRM TEAM RECOMMENDATIONS IN TIER II AND SEE IF THERE'S A DESIRE TO ACCEPT THOSE RECOMMENDATIONS. AND THEN WE'LL LOOK AT THE REMAINDER OF TIER II -- WELL, TIER III. WE ONLY HAVE TWO TIERS, I AND III, OR THE REST OF TIER II AND SEE IF WE CAN MOVE THAT UP OR NOT FUND THOSE.

SO THE FIRST MOTION, IS THERE A MOTION TO MOVE ANY APPLICATION OUT OF TIER I? OKAY. THEN LET'S TAKE UP 09073. IS THERE A MOTION TO ACCEPT THE CIRM TEAM RECOMMENDATION AND MOVE THAT INTO TIER I?

DR. HIGGINS: SO MOVED.

DR. JUELSGAARD: I SO MOVE.

MR. SHEEHY: LOOKS LIKE WE'VE GOT TWO, DAVID HIGGINS, AND WHO IS THE OTHER?

DR. JUELSGAARD: THIS IS STEVE, BUT I'LL SECOND.

MR. SHEEHY: OKAY. THEN THAT'S A SECOND.

DO WE HAVE ANY DISCUSSION OF THIS? ANY COMMENTS, QUESTIONS? DO WE HAVE ANY PUBLIC COMMENT ON THIS? MARIA, DO YOU WANT TO CALL THE ROLL THEN.

MS. BONNEVILLE: JEFF, THERE'S PUBLIC COMMENT HERE IN SAN DIEGO.

MR. SHEEHY: OKAY. GREAT. GREAT.

MS. RAUB: HI, EVERYBODY AND EVERYONE HERE. MY NAME IS JENIFER RAUB. I'M PRESIDENT OF THE SUMMIT4STEMCELL FOUNDATION, A PATIENT ADVOCATE FOR PARKINSON'S DISEASE, AND AN AMBASSADOR FOR AMERICANS FOR CURES. I'VE HAD PARKINSON'S FOR OVER TEN YEARS, AND I FEEL IT EVERY SINGLE DAY, BUT I'D LIKE TO THANK SUPERVISOR DAVE ROBERTS FOR HIS

SUPPORT, CIRM, THE ICOC, AND THE STAFF FOR THEIR TIME AND EFFORTS. I'D ALSO LIKE TO THANK EVERYONE IN THIS ROOM FOR BEING HERE TODAY IN SUPPORT.

ON BEHALF OF SUMMIT4STEMCELL AND THE PARKINSON'S'S COMMUNITY, I URGE THE ICOC TO PLEASE VOTE TO FUND THIS AUTOLOGOUS CELL THERAPY RESEARCH FOR PARKINSON'S. I RECEIVE CALLS FROM ALL OVER THE COUNTY, THE STATE, THE NATION, AND INTERNATIONALLY FROM PEOPLE DESPERATE FOR SOMETHING OTHER THAN THE MEDICATIONS THAT A LOT OF US KNOW THAT JUST STOP WORKING. THEY WANT A STEM CELL-BASED THERAPY. THEY WANT A LEGITIMATE STEM CELL THERAPY.

WHEN I EXPLAIN THE RESEARCH ABOUT USING THEIR SKIN CELLS TO CREATE DOPAMINE-PRODUCING NEURONS, MOST OFTEN THEY GO SILENT, A LOT OF TIMES THEY CRY, AND THEN THEY THANK ME FOR GIVING THEM SOMETHING TO HANG ONTO, FOR GIVING THEM HOPE. THIS RESEARCH PROVIDES MORE THAN HOPE. THIS RESEARCH COULD PROTECT PEOPLE FROM (INAUDIBLE), POTENTIALLY PROTECT OVER 7 MILLION LIVES, AND YOUR VOTE TODAY COULD MAKE THIS PARKINSON'S PROJECT ONE OF THE BIGGEST JEWELS IN CIRM'S CROWN.

I'D ALSO LIKE TO ASK EVERYONE HERE IN SUPPORT OF SUMMIT, DR. LORING, DR. HOUSER, AND DR. BRATT-LEAL TO PLEASE STAND. SEE HOW MANY WE

HAVE. WOW. WHAT DO YOU THINK? 50? 40? I THINK WE'RE CLOSE TO 50 STANDING RIGHT NOW. THANK YOU.

PEOPLE'S LIVES ARE THE REAL ISSUE HERE. EVERY PERSON IN THIS ROOM IS SOMEHOW AFFECTED BY PARKINSON'S DISEASE. PARKINSON'S DOES NOT WAIT FOR DEBATE, DISCUSSION, OR A VOTE. PARKINSON'S SIMPLY KEEPS CREEPING FORWARD. THESE PEOPLE ARE FADING AWAY. THESE PEOPLE DESPERATELY WANT TO BE WELL, TO END THE UGLINESS OF PARKINSON'S, TO MOVE WITHOUT PAIN, STIFFNESS, OR TREMORS, AND TO BE ABLE TO CONTROL THEIR MOVEMENTS. THEY WANT TO MOVE.

DR. LORING, DR. HOUSER, AND DR. BRATT-LEAL CAN DO ALL OF THAT. I IMPLORE YOU, WE ALL IMPLORE YOU TO PLEASE FUND THIS. LET'S COLLABORATE AND PROVIDE A SAFE, EFFICACIOUS, AND LEGITIMATE AUTOLOGOUS-BASED CELL THERAPY FOR ALL PATIENTS WITH PARKINSON'S DISEASE BEGINNING TODAY. THANK YOU.

(APPLAUSE.)

MR. SHEEHY: THANK YOU, MS. RAUB. AND THANK YOU TO EVERYBODY IN ATTENDANCE IN SAN DIEGO. IT'S REALLY FABULOUS TO HAVE EVERYBODY TAKE AN INTEREST IN WHAT CIRM IS DOING.

ARE THERE MORE PUBLIC COMMENTS? IS THERE MORE PUBLIC COMMENT?

MS. BONNEVILLE: NOT HERE, JEFF.

MR. SHEEHY: SHOULD WE CALL THE ROLL THEN?
MS. BONNEVILLE: ANNE-MARIE DULIEGE.
DR. DULIEGE: YES.
MS. BONNEVILLE: DAVID HIGGINS.
DR. HIGGINS: YES.
MS. BONNEVILLE: STEVE JUELSGAARD.
DR. JUELSGAARD: YES.
MS. BONNEVILLE: SHERRY LANSING. KATHY LAPORTE.
MS. LAPORTE: YES.
MS. BONNEVILLE: LAUREN MILLER.
MS. MILLER: YES.
MS. BONNEVILLE: ADRIANA PADILLA.
DR. PADILLA: YES.
MS. BONNEVILLE: JOE PANETTA.
MR. PANETTA: YES.
MS. BONNEVILLE: FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: YES.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: YES, EXCEPT FOR THOSE WITH WHICH I'M IN CONFLICT.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART.

MR. TORRES: TORRES, AYE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MS. BONNEVILLE: MOTION CARRIES.

(APPLAUSE.)

MR. SHEEHY: SO DO I HAVE A MOTION TO MOVE -- TO ACCEPT THE CIRM TEAM RECOMMENDATION AND MOVE 08982 INTO THE FUNDABLE CATEGORY?

DR. JUELSGAARD: THIS IS STEVE JUELSGAARD. SO MOVED.

MR. SHEEHY: DO I HAVE A SECOND?

MR. TORRES: SECOND.

MR. SHEEHY: IS THERE ANY DISCUSSION OR COMMENT? IS THERE ANY PUBLIC COMMENT AT ANY OF THE SITES? SO MARIA, COULD YOU CALL THE ROLL FOR THIS PLEASE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.
DR. JUELSGAARD: YES.
MS. BONNEVILLE: KATHY LAPORTE.
MS. LAPORTE: YES.
MS. BONNEVILLE: LAUREN MILLER.
MS. MILLER: YES.
MS. BONNEVILLE: ADRIANA PADILLA.
DR. PADILLA: YES.
MS. BONNEVILLE: JOE PANETTA.
MR. PANETTA: YES.
MS. BONNEVILLE: FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: YES.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MS. BONNEVILLE: MOTION CARRIES.

MR. SHEEHY: GREAT. SO IS THERE A MOTION TO MOVE ANY OTHER PROJECT IN TIER II INTO THE FUNDABLE CATEGORY, TIER I? THEN IF THERE IS NONE, WE NEED AN OMNIBUS MOTION THAT WOULD FUND ALL THE PROJECTS IN TIER I PLUS 09073 AND 08982 AND NOT TO FUND THE REMAINDER OF THE PROJECTS LISTED IN TIER II. AND THAT NEEDS TO COME, BOTH THE MOTION AND THE SECOND, FROM SOMEONE WITHOUT A CONFLICT. AM I CORRECT THERE, JAMES?

MR. HARRISON: YOU ARE ABSOLUTELY CORRECT. THANKS FOR THE REMINDER, JEFF.

MR. TORRES: TORRES MOVES.

DR. PRIETO: I'LL SECOND.

MR. SHEEHY: SO SENATOR TORRES AND THEN DR. PRIETO ARE THE MOTION MAKER AND THE SECOND.

AND THEN, JAMES, COULD YOU REMIND US OF THE FORM WE SHOULD ANSWER IN THE EVENT THAT WE HAVE A CONFLICT IN ANY OF THESE APPLICATIONS.

MR. HARRISON: YES. COULD YOU PLEASE VOTE EITHER YES OR NO EXCEPT FOR THOSE APPLICATIONS IN WHICH YOU HAVE A CONFLICT.

MR. SHEEHY: GREAT. SO MARIA, --

DR. SAMBRANO: MR. SHEEHY, WE HAVE PUBLIC

COMMENT.

MR. SHEEHY: I WAS GOING TO SAY WE'RE GOING TO HAVE PUBLIC COMMENT.

DR. SAMBRANO: WE HAVE PUBLIC COMMENT IN OAKLAND.

DR. SCHUELE: DEAR DISTINGUISHED ICOC MEMBERS, I'M VERY EXCITED TO BE HERE TODAY AND THANK YOU FOR YOUR HEART WARMTH TO ENABLE NEW STEM CELL THERAPIES FOR INCURABLE DISEASES. MY NAME IS BIRGITT SCHUELE, AND I'M THE INVESTIGATOR AT THE PARKINSON'S INSTITUTE AND CLINICAL CENTER.

I WANTED TO TAKE A MINUTE OF YOUR TIME TO UPDATE YOU ON NEW, REALLY IMPORTANT DATA WITH REGARDS TO OUR APPLICATION. I ALSO SUBMITTED A LETTER WITH MORE DETAILS TO YOU.

OUR DISC2 GRANT APPLICATION PROPOSES TO DEVELOP A NOVEL DISEASE-MODIFYING THERAPY FOR PARKINSON'S DISEASE. WHILE OUR PROPOSAL RECEIVED FAVORABLE CRITIQUES FROM THE GRANTS WORKING GROUP, THE REVIEWERS FELT THAT MORE PRELIMINARY DATA WOULD BE CRITICAL TO SHOW THE FEASIBILITY OF OUR PROPOSED STUDY.

WHILE OUR GRANT WAS UNDER REVIEW, NEW DATA WERE PUBLISHED THAT NOW ESTABLISH THE VIABILITY OF OUR APPROACH USING DATA FROM A GROUP IN OXFORD

DESCRIBE THE SUCCESSFUL USE OF CRISPR TECHNOLOGY FOR THE KNOCKDOWN OF THE PARKINSON'S GENE ALPHA-SYNUCLEIN AS WE HAVE PROPOSED IN OUR APPLICATION. THE DESIGN THAT WORKS BEST IN THEIR HANDS WAS ACTUALLY OUR HIGHEST RANKED PREDICTED CONSTRUCT. THESE NEW DATA SHOW THE FEASIBILITY OF OUR STUDY AND ALSO SUBSTANTIALLY MIRRORS THEIR PROJECT.

SO IT WILL ALLOW US TO MOVE FASTER ON THESE DATA. FIRST, WE CAN QUICKLY MOVE THE NOVEL CONSTRUCT NOW INTO IN VIVO STUDIES; AND THEN, SECOND, WE CAN POSSIBLY DESIGN EVEN BETTER CONSTRUCT THAT COULD ACHIEVE HIGHER KNOCKDOWN FOR THIS PARKINSON'S GENE.

PLEASE CONSIDER THIS INFORMATION WHEN YOU'RE MAKING YOUR FINDING DECISION.

I ALSO HAVE MR. BART NARGER HERE WHO WILL DESCRIBE HIS PERSPECTIVE ON THE NEED FOR NOVEL PARKINSON'S THERAPY. THANK YOU.

MR. NARGER: HELLO, EVERYONE. MY NAME IS BART NARGER, AND I WAS DIAGNOSED WITH PARKINSON'S ON DECEMBER 6TH OF 2011, NEARLY FIVE YEARS AGO. I'VE BEEN LUCKY THAT I'VE BEEN ABLE TO STEP AWAY FROM WORK AND REALLY FOCUS ON MY HEALTH.

PARKINSON'S DISEASE IS THE THIRD FASTEST

GROWING CAUSE OF DEATH IN THE UNITED STATES AFTER ALZHEIMER'S AND HYPERTENSION. THERE ARE ABOUT 60,000 CASES DIAGNOSED EACH YEAR. CURRENTLY THE ONLY TREATMENT THAT EXISTS ARE ABOUT SYMPTOM SUPPRESSION. THERE'S NOTHING THAT ACTUALLY WORKS ON THE CORE OF THE DISEASE ITSELF.

SO PRIMARILY WHAT WE'RE DOING IS WE'RE PUTTING OUR FINGERS IN THE DIKE, AND THE WATER KEEPS ON RISING AND RISING, MEANING I HAVE FEWER AND FEWER NEURONS PRODUCING DOPAMINE EVERY DAY NO MATTER WHAT THE MED.

I'M TAKING FIVE MEDICATIONS RIGHT NOW: RYTARY, ARTANE, SELEGILINE, PRAMIPEXOLE, AND AMANTADINE, AND NONE OF THESE DRUGS DOES ANYTHING ABOUT THE PROGRESSION OF THE DISEASE. THEY MERELY SUPPRESS SYMPTOMS.

SO AS ONE MOVES DOWN THE PATH OF PARKINSON'S DISEASE AND AS THE DISEASE PROGRESSES, ONE NEEDS TO TAKE MORE AND MORE PILLS BECAUSE YOU'RE FILLING A BIGGER AND BIGGER GAP. I ACTUALLY GOT TO THE POINT WHERE MY NEUROLOGIST RECOMMENDED DEEP BRAIN STIMULATION. A NEUROSURGEON PUTS TWO PROBES INTO THE SUBTHALMAL NUCLEUS IN THIS CASE AND STIMULATES IT TO HELP SUPPRESS SYMPTOMS. I HAD THIS SURGERY, IT WORKED GREAT, THEN THERE WAS AN

INFECTION, AND WE HAD TO YANK IT OUT AGAIN. SO I'M CURRENTLY WITHOUT THAT. AND, AGAIN, I WENT THROUGH ALL THIS JUST TO SUPPRESS SYMPTOMS. THERE'S NOTHING OUT THERE THAT HELPS REDUCE THE PROBLEM, THE ROOT CAUSE, OF PARKINSON'S, WHICH MOST SCIENTISTS BELIEVE IT'S BASED ON THE ALPHA ALPHA-SYNUCLEIN, WHICH KIND OF BUNCHES UP AND KILLS THE NEURONS IN THE BRAIN.

SO DR. SCHUELE'S TEAM AT THE PARKINSON'S INSTITUTE IS PROPOSING AN APPROACH IN HUMAN-DERIVED STEM CELLS FROM THE PATIENT'S SKIN CELLS AS PROOF OF CONCEPT FOR FURTHER CLINICAL DEVELOPMENT. IT'S A UNIQUE STUDY THAT WILL PREVENT ALPHA-SYNUCLEIN FROM BEING MADE IN EXCESS TO PROTECT NEURONS IN THE BRAIN. WE NEED TO DO MORE THAN MERELY SUPPRESS SYMPTOMS, BUT ATTACK THE ROOT CAUSE OF PARKINSON'S DISEASE OR, EVEN BETTER, REPAIR THE DAMAGE THAT PARKINSON'S DISEASE HAS BROUGHT.

AGAIN, THERE'S NOTHING OUT THERE FOR PARKINSON'S DISEASE THAT WILL DO ANYTHING BUT SUPPRESS SYMPTOMS, NOT GO AFTER ROOT CAUSES.

MS. CHEUNG: JEFF, I BELIEVE THERE'S ALSO PUBLIC COMMENT AT DIANE'S LOCATION.

MR. SHEEHY: DIANE. WE HAVE SOME BACKGROUND PROBLEMS.

MS. CHEUNG: SORRY. IT WAS NOT FOR THAT

APPLICATION.

DR. CONKLIN: THIS IS BRUCE CONKLIN CALLING, AND I AM SPEAKING ON BEHALF OF THE 08990. THIS IS THE HUMAN HEART ON A CHIP FOR DRUG DISEASE MODELING. THIS APPLICATION RECEIVED A SCORE OF 85 -- SORRY -- 83 AND A MEDIAN OF 82, I BELIEVE. AND SO ACTUALLY IT WAS -- THE COMMITTEE HAS ALREADY ACTUALLY DECIDED TO FUND SCORES ABOVE AND JUST BELOW THIS IN RECENT -- JUST IN DISCUSSION THIS MORNING. SO IT SCORES VERY WELL.

THE MAIN CRITICISM OF THIS -- I SHOULD ADD THAT HEART DISEASE IS THE NO. 1 KILLER IN THE UNITED STATES AND IS A MAJOR CONCERN FOR THE CIRM. I SHOULD SAY THAT THIS PROJECT USES HUMAN IPS CELLS AS THE MODEL SYSTEM AND USES STATE-OF-THE-ART TECHNIQUES OF GENE EDITING TO IDENTIFY MODELS TO TEST IN THE STATE-OF-THE-ART HEART ON A CHIP TECHNOLOGY DEVELOPED BY THE HEALY LAB.

THE PRIMARY CONCERN OF THE REVIEW WAS THAT THERE WAS CONCERN ABOUT THE STATE OF DIFFERENTIATION OF THE CARDIAC MYOCYTES, LIKE ACTUALLY THE ENTIRE FIELD OF IPS DIFFERENTIATION, THE CELLS DO NOT REACH A FULLY MATURE STATE, AND THIS IS NOT SOMETHING WHICH IS UNIQUE TO CARDIAC MYOCYTES, BUT ALSO FOR THE PANCREATIC ISLET CELLS AND NEURONS AND OTHER

DISEASE SYSTEMS WHICH ARE USED AND ACTIVELY FUNDED BY THE CIRM.

HOWEVER, ONE THING WHICH IS REALLY -- THAT IS, ALTHOUGH WE ARE WORKING CONTINUOUSLY TO ACTUALLY ADDRESS THAT PROBLEM, ONE WAY TO ADDRESS THE PROBLEM IS ACTUALLY TO PUT THE CELLS INTO A HEART ON A CHIP MODEL BECAUSE ACTUALLY THE CELLS, WHEN THEY'RE IN A TISSUE, THEY BECOME MORE MATURE AND, IN FACT, DR. HEALY AND HIS GROUP, WHICH I COLLABORATE WITH CLOSELY, ACTUALLY SHOWS THAT THE CELLS ACTUALLY HAD A MORE MATURE RESPONSE. SO ALTHOUGH IT WAS A CRITICISM OF THE REVIEWERS, IT'S ACTUALLY BEING DIRECTLY ADDRESSED BY THIS APPLICATION.

AND THIS IS SHOWN BY DRUG RESPONSES WHICH ARE MORE HUMANLIKE AND ADULTLIKE ON THE HEART ON A CHIP THAN IN THE -- WHEN THE CELLS ARE JUST IN A PLATE ESSENTIALLY.

I SHOULD ADD THAT THE CARDIAC MYOCYTES THEMSELVES ARE -- WE'RE USING THE EXACT SAME PROTOCOL FOR DIFFERENTIATION AS CIRM-FUNDED PROGRAMS AND NIH-FUNDED PROGRAMS FOR USING THE CELLS FOR TRANSPLANTATION AND CELLS TO TEST THERAPY. I THINK THAT THIS PROGRAM ITSELF, MORE IMPORTANTLY, I THINK, IN TERMS OF THE IMPORTANCE OF THIS PROGRAM, IS THAT WE ARE ACTUALLY ADDRESSING A CRITICAL ISSUE WHICH IS

DRUG TOXICITY. DRUGS THAT ARE BEING USED FOR CANCER CHEMOTHERAPY, FOR INSTANCE, INCREASINGLY IT'S DOSE LIMITING TO GIVE THE DRUGS. FOR INSTANCE, FOR SEPTIN IT'S DOSE LIMITING; FOR MANY OTHER DRUGS IT'S DOSE LIMITING.

MS. CHEUNG: EXCUSE ME. DR. CONKLIN, YOUR THREE MINUTES ARE UP.

DR. CONKLIN: OKAY. THANK YOU VERY MUCH. SO THANK YOU FOR LISTENING TO ME. SORRY I WENT OVER.

MR. SHEEHY: THANK YOU. DO WE HAVE ADDITIONAL PUBLIC COMMENT?

DR. HIGGINS: JEFF, THIS IS DAVID HIGGINS. CAN I MAKE A COMMENT?

MR. SHEEHY: SURE.

DR. HIGGINS: I THINK IT'S TEMPTING THAT WE'VE RAISED -- WE SORT OF RESCUED TWO GRANT PROPOSALS AND FUNDED THEM TO CONSIDER ALL COMERS EQUALLY. I'D JUST LIKE TO POINT OUT THAT THE TWO THAT WE RESCUED HAD VAST MAJORITIES OF THE GWG SCIENTIFIC GROUP APPROVING THEM AND PUTTING THEM IN TIER I, IN BOTH CASES 10 OUT OF 14.

THERE'S A LOT OF WAYS YOU CAN SLICE AND DICE HOW YOU FEEL ABOUT RESCUING A GRANT, BUT I JUST WANTED TO POINT OUT THAT THOSE TWO WERE UNIQUE IN

THE ENTIRE TIER II GROUP, THAT THEY HAD SUCH A LARGE MAJORITY OF THE SCIENTIFIC COMPONENT OF THE GWG SUPPORT.

MR. SHEEHY: THANK YOU, DAVID. DO WE HAVE ANY OTHER COMMENTS, QUESTIONS, PUBLIC COMMENT? SO WE HAVE A MOTION ON THE FLOOR. AND SO, MARIA, COULD YOU CALL THE ROLL. AND REMEMBER IF FOLKS HAVE A CONFLICT, YOU SHOULD ACKNOWLEDGE THAT IN VOTING.

MS. LAPORTE: COULD YOU JUST RESTATE THE MOTION PLEASE.

MR. SHEEHY: SURE. THE MOTION IS TO FUND ALL THE APPLICATIONS IN TIER I PLUS THE TWO APPLICATIONS THAT WERE RECOMMENDED FOR FUNDING BY THE CIRM TEAM, 09073 AND 08982.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: AYE.

MR. SHEEHY: AND THE OTHER PART -- LET ME JUST -- AND THE OTHER PART IS TO NOT FUND ANY OF THE APPLICATIONS IN TIER II. SO GO AHEAD.

DR. DULIEGE: SO I VOTE YES EXCEPT FOR ANY APPLICATIONS I MAY BE IN CONFLICT WITH.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: SHERRY LANSING. KATHY LAPORTE.

MS. LAPORTE: YES.

MS. BONNEVILLE: EXCEPT FOR THOSE WITH WHICH YOU HAVE A CONFLICT.

MS. LAPORTE: YES, EXCEPT IF I HAVE A CONFLICT.

MS. BONNEVILLE: LAUREN MILLER. ADRIANA PADILLA.

DR. PADILLA: YES.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: YES.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES, AND I HAVE NO CONFLICTS.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: YES.

MS. BONNEVILLE: JEFF SHEEHY.

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

MS. BONNEVILLE: THANK YOU. OS 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: DIANE WINOKUR.

MS. WINOKUR: YES EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: THANK YOU. MOTION CARRIES.

MR. SHEEHY: GREAT. THANK YOU.

OKAY. NEXT WE HAVE THE CHALLENGE GRANT ROUND. SO, DR. SAMBRANO, WOULD YOU LIKE TO TAKE US THROUGH THAT.

DR. SAMBRANO: YES. THANK YOU. SO I'LL TRY TO BE QUICK. THE OBJECTIVE OF THE CHALLENGE PROGRAM IS TYPICALLY WHEN WE HAVE A UNIQUE QUESTION OR IF THERE IS A NEED OR BOTTLENECK THAT WE WANT TO ADDRESS IN THE FIELD. THE CHALLENGE PROGRAM ALLOWS US TO PRESENT SUCH A CHALLENGE, IF YOU WILL, SO THAT WE GET PROPOSALS TO TRY TO ADDRESS THEM.

IN THIS CASE THIS IS THE FIRST CHALLENGE COMPETITION THAT WE HAVE HAD, AND SO THE CHALLENGE HERE WAS AN ATTEMPT TO ENHANCE THE VALUE OF CIRM'S IPSC BANK FOR DISEASE MODELING, TARGET DISCOVERIES, AND SO ON BY ACQUIRING AND ADDING GENETIC DATA FOR THE UP TO 3,000 DISEASE-SPECIFIC AND CONTROL LINES

THAT WOULD BE DEVELOPED UNDER THE IPSC PROGRAM.

SO SOME KEY POINTS HERE: WE WERE LOOKING FOR A SINGLE GRANTEE THAT WOULD ACCOMPLISH THIS. THE OVERALL DELIVERABLE OF THE PROJECT IS A COMPREHENSIVE GENETIC PROFILE OF CIRM'S IPSC BANK LINES THAT WILL HOPEFULLY SERVE AS A CATALYST TO FURTHER STUDY AND INTEREST IN THESE CELLS.

WE DID NOT SPECIFY EXACTLY WHAT THE GENETIC PROFILES HAD TO ENTAIL, SO THAT WAS LEFT FLEXIBLE FOR APPLICANTS TO BOTH TELL US HOW THEY WOULD DO THIS AND WHY THAT WOULD PROVIDE VALUE TO THE IPSC BANK.

AGAIN, THE SAME REVIEW CRITERIA IN THIS CASE: THE SIGNIFICANCE AND IMPACT; THAT IS, HOW IT WOULD DIRECTLY ADDRESS THE CHALLENGE THAT WE POSED, WHETHER THE APPROACHES THAT ARE PROPOSED ARE APPROPRIATE AND MAKE SENSE, AND WHETHER THEY HAVE A GOOD DESIGN AND ARE LIKELY TO ACCOMPLISH IT.

AGAIN, A REMINDER, THE SCORING CHANGES A LITTLE BIT AGAIN. THE SCORING SYSTEM HERE IS 1 TO 100, 100 BEING THE BEST POSSIBLE SCORE. HOWEVER, ONLY THE APPLICATION WITH THE HIGHEST AVERAGE SCORE CARRIES THE RECOMMENDATION OF THE GRANTS WORKING GROUP TO FUND BECAUSE THIS IS A PROGRAM WHERE WE CAN ONLY -- INTEND TO FUND ONLY ONE APPLICATION.

SO IN THE NEXT SLIDE THERE'S THE TABLE WHICH SHOWS A LISTING OF THE FIVE APPLICATIONS THAT WERE REVIEWED, AND THE APPLICATION THAT SCORED THE HIGHEST WITH A SCORE OF 88 IS 9167 WITH A BUDGET OF 2 MILLION, WHICH IS THE AMOUNT THAT WE ALLOCATED TO THIS PROGRAM. SO IF THERE ARE QUESTIONS, I'D BE HAPPY TO TAKE THEM.

MR. SHEEHY: SO COULD I TURN THE CHAIR OVER TO OS IF HE'D BE WILLING TO TAKE IT, DR. STEWARD, BECAUSE I WANTED TO MAKE A MOTION ON THIS PARTICULAR ROUND. ARE YOU COMFORTABLE WITH THAT, OS?

DR. STEWARD: SORRY. YES, I CAN DO THAT. SO CAN WE HEAR A MOTION?

MR. SHEEHY: SO THE MOTION I WANTED TO MAKE WAS NOT TO FUND ANY OF THE APPLICATIONS IN THIS ROUND. AND THE REASON IS, FIRST, I THINK THAT WE'VE SPENT $25 MILLION ALREADY ON THE REPOSITORY. WE SPENT 40 MILLION ON THE GENOMICS CENTER. AND THIS 2 MILLION IS JUST THE BEGINNING OF WHAT WE WOULD NEED TO SPEND TO ENHANCE THIS REPOSITORY. AND I THINK WE'VE INVESTED ENOUGH IN BOTH THE REPOSITORY AND GENOMICS AT LEAST AT THIS POINT.

WE HAVE 3,000 LINES, SO EVEN THE APPLICATION THAT'S SUCCESSFUL DOESN'T PROPOSE TO DO

MORE THAN A THOUSAND OF THOSE LINES. SO AT SOME POINT WE'LL NEED SOME ADDITIONAL MILLIONS TO DO THE REST OF THE LINES.

ONE OF THE REVIEWERS AT THE REVIEW SAID THAT THEY WOULD BE, EVEN WITH THIS GENOMIC ANALYSIS OF THESE LINES, THEY WOULD BE UNABLE TO USE THESE MATERIALS IN RESEARCH FUNDED BY THE NIH BECAUSE THEY'RE NOT DOING A GENOMIC ANALYSIS OF THE SOURCE TISSUE.

SO THE IDEA HERE IS THEY'RE GOING TO ANALYZE THE STEM CELL LINES AS THEY KIND OF CAPTURE THE CHANGES AS THEY GO DOWN THE PATHWAYS. SO WITHOUT AN UNDERSTANDING OF WHAT THE ORIGINAL MATERIAL LOOKED LIKE, THEN THOSE CHANGES ARE VERY HARD, AT LEAST IT WOULD BE VERY DIFFICULT TO GET RESEARCH FUNDED TO LOOK AT THOSE LINES NOT KNOWING WHERE THEY CAME FROM, NOT HAVING THAT SAME ANALYSIS WHERE THEY CAME FROM.

SO ONE SUGGESTION THAT CAME OUT OF THE REVIEW WAS THAT WE FUND LOOKING AT THE SOURCE MATERIAL -- FUND THE GENOMIC ANALYSIS OF THE SOURCE MATERIAL AS WELL. ANOTHER REVIEWER SUGGESTED THAT WE FUND BOTH OF THE TOP TWO TO DO THE SAME WORK BECAUSE THERE COULD BE VARIATIONS IN THE GENOMIC ANALYSIS OF EACH SERIES. SO THE RESEARCH BASICALLY

TO BE VALIDATED WOULD BE BEST IF WE ACTUALLY FUNDED BOTH TO VALIDATE THE FINDINGS OF THE FIRST GROUP.

SO WHAT COMES TO MIND HERE IS THAT WE'VE GOT THIS RESOURCE, TWO COMMERCIAL ENTITIES. ONE OF THE COMMERCIAL ENTITIES HAS BEEN ACQUIRED BY A MULTINATIONAL FUJI FILM, CDI HAS BEEN ACQUIRED BY THAT. SO THERE IS A LOT OF MONEY ON THAT SIDE OF THE TABLE, A LOT OF COMMERCIAL MONEY. AND THIS IS REALLY A COMMERCIAL PRODUCT. AND FOR US TO DO THIS INVESTMENT WOULD BE JUST A PARTIAL INVESTMENT.

I DON'T BELIEVE THAT IT'S CIRM'S ROLE TO CONTINUE TO PUT FUNDS INTO THIS PROJECT TO MAKE IT MORE COMMERCIALLY VIABLE. IF IT'S COMMERCIALLY VIABLE, THERE ARE ENTITIES WITH MUCH DEEPER POCKETS THAT COULD TAKE THESE CELL LINES --

(INTERRUPTION.)

MR. SHEEHY: SO THAT'S WHY I'M MAKING MY MOTION NOT TO FUND THESE. IF THERE'S A SECOND, THAT WOULD BE GREAT. BUT ALSO I UNDERSTAND OTHERS MAY HAVE COMMENTS.

DR. STEWARD: THANK YOU, JEFF.

(INTERRUPTION.)

DR. STEWARD: WE HAVE A MOTION. DO WE HAVE A SECOND?

DR. PRIETO: I'LL SECOND.

DR. STEWARD: IS THERE DISCUSSION?

MR. TORRES: YES. I HAVE A QUESTION OF GIL. HOW MUCH DO YOU FORESEE, IF ANY, RETURN TO THE STATE OF CALIFORNIA AS A RESULT OF A COMMERCIAL PRODUCT THAT THEY'RE TALKING ABOUT HERE?

DR. SAMBRANO: THE GOAL OF THIS CHALLENGE PROGRAM IS TO TRY TO ADD VALUE TO SOMETHING THAT IS ALREADY UNDER WAY. SO THE IPSC BANK IS GENERATING IPSC LINES. IT IS NOT YET DONE, BUT ONE OF THE THINGS THAT WE HAD THOUGHT OF THAT COULD MAKE THEM MORE ATTRACTIVE AND VALUABLE TO INVESTIGATORS WHO WOULD UTILIZE THEM WAS TO PROVIDE GENETIC DATA OR INFORMATION ABOUT EACH OF THE LINES. YOU KNOW, WHETHER ULTIMATELY THAT ENDS UP BEING A TRUE OUTCOME, WE DON'T KNOW. BUT IT IS SOMETHING THAT, BASED ON DISCUSSIONS WITH OTHER INVESTIGATORS WHO WOULD UTILIZE THEM, THEY FELT THAT THAT WAS AN ASPECT THAT WOULD ADD VALUE AND A REASON TO GET IT.

PAT OLSON MAY HAVE ADDITIONAL INFORMATION.

DR. OLSON: I JUST WANTED TO SPEAK TO A COUPLE OF COMMENTS. FIRST, AS WAS POINTED OUT BY MR. SHEEHY, CDI IS, IN FACT, WAS ACQUIRED BY FUJI FILM. HOWEVER, CDI BASICALLY HAS RESPONSIBILITY ONLY FOR MAKING THE LINES, AND THEY MAKE THEM SO THAT THEY'RE ALL MADE THE SAME WAY.

THE PEOPLE WHO ACTUALLY HAVE RESPONSIBILITY FOR DISTRIBUTING THE LINES IS A NONPROFIT BANK CORIELL. AND WHAT CORIELL HAS FOUND IS THAT IN THE REQUEST FOR THE LINES, AND THEY ARE BEING REQUESTED NOW, THEY ARE BEING SOLD, ONE OF THE THINGS THAT KEEPS COMING UP IS WHAT GENETIC INFORMATION IS THERE THAT'S ASSOCIATED. THE PEOPLE WOULD REALLY LIKE TO SEE THAT. SO IN POINT OF FACT, ALL THE LINES WILL ACTUALLY HAVE A SNP WHICH IS LOOKING AT A LOT OF LOCI THAT ARE ASSOCIATED WITH DISEASE. ALL THE LINES WILL HAVE THAT ANALYSIS ASSOCIATED WITH THEM, AND THEN A SUBSET OF THE LINES WILL HAVE A GOLD GENOMIC ANALYSIS ASSOCIATED WITH THEM.

SO THERE WILL BE GENETIC INFORMATION ASSOCIATED WITH ALL THE LINES. THEY ARE GOING TO BE MADE AVAILABLE BY A NONPROFIT ORGANIZATION, AND OBVIOUSLY OUR EXPECTATION IS THAT, IN POINT OF FACT, THIS KIND OF RESEARCH WOULD BE VERY VALUABLE TO COMMERCIAL ENTITIES WHO ACTUALLY HAVE DIFFERENT TERMS FROM NONPROFIT ENTITIES IN THE ACQUISITION OF THE LINES AND THAT THEIR USE BY COMMERCIAL ENTITIES COULD AT SOME POINT RETURN VALUE.

BUT, AGAIN, ONE OF THE THINGS THAT CORIELL HEARS FROM THEIR CUSTOMERS IS THE IMPORTANCE OF THE

GENETIC INFORMATION.

MR. TORRES: THANK YOU.

MR. SHEEHY: SO, OS, COULD I JUST MAKE A COMMENT?

DR. STEWARD: YES, PLEASE.

MR. SHEEHY: SO WE'RE ONLY GOING TO HAVE THE GENETIC ANALYSIS ON A SUBSET OF THE LINES THAT WE'RE DEVELOPING. I JUST -- THIS SEEMS LIKE THE BEGINNING -- AT SOME POINT WE HAVE TO DECIDE HOW MUCH WE WANT TO INVEST IN THIS PROJECT. IF WE DO THIS, I THINK IT JUST MAKES SENSE THAT WE'LL COME BACK AGAIN FOR ADDITIONAL MILLIONS OF DOLLARS AND AGAIN FOR ADDITIONAL MILLIONS OF THE DOLLARS. SO THE REFINEMENT OF THIS TOOL, WHICH RIGHT NOW IS A BASIC RESEARCH TOOL, AS I KIND OF UNDERSTAND IT, DOESN'T -- AT SOME POINT FOR THESE BIG INFRASTRUCTURE THINGS, IT SEEMS LIKE IT'S A LONG WAY FROM THE CLINIC, AND IT'S NOT TO GOING TO BE COMPLETE UNTIL WE INVEST AN UNCERTAIN AMOUNT OF ADDITIONAL MONEY.

SO WE GENERATED THE LINES. I JUST FEEL LIKE SOMEONE ELSE CAN CONTINUE TO FUND THIS PART OF IT. WE'VE PUT $40 MILLION IN THE GENOMIC CENTER. SO IT JUST SEEMS SOMEWHAT UNUSUAL THAT AFTER $65 MILLION WE NEED TO KEEP PUTTING MORE INTO THIS. AT

SOME POINT THESE ARE SOFT COSTS AND THE MARGINAL COST OF GOING FORWARD WITH AN UNCERTAIN OUTCOME OF THE UTILITY OF THESE CELLS JUST MAKES ME HESITATE TO INVEST IN IT.

DR. STEWARD: THANKS, JEFF. DO WE HAVE ANY OTHER COMMENTS?

MS. WINOKUR: YES. DIANE.

DR. STEWARD: GO AHEAD, DIANE.

MS. WINOKUR: I JUST WANTED TO COMMENT THAT, AND IT'S SOMETHING I'M SURE YOU ALL KNOW, BUT DESIGNATING AN ORGANIZATION LIKE CLAMAYA (PHONETIC), A NONPROFIT, IS A TAX DESIGNATION. IT DOESN'T MEAN THE MONEY DOESN'T GO TO SUPPORT STAFF OR BUILDING OR ANY NUMBER OF THINGS. SO IT DOESN'T MEAN THAT THERE'S FUNDING THAT GOES TO THE ORGANIZATION.

DR. STEWARD: THANK YOU, DIANE. OTHER COMMENTS?

DR. JUELSGAARD: OS, THIS IS STEVE. CAN WE HAVE THE -- I KNOW PAT SPOKE TO THIS. I GUESS ACTUALLY I DON'T HAVE A QUESTION. SHE'S ALREADY ANSWERED IT FOR ME. THANKS.

DR. OLSON: AGAIN, I JUST WANT TO REITERATE THAT THE SNP ANALYSIS, WHICH LOOKS AT MANY DIFFERENT GENETIC LOCI, WILL BE PERFORMED ON ALL THE LINES, BUT A SUBSET OF THE LINES WILL HAVE A FULL

GENETIC -- A FULL GENOMIC ANALYSIS, A FULL SEQUENCING ANALYSIS, THAT THAT INFORMATION IS DEEMED TO BE VALUABLE, EVEN THE SNP ANALYSIS, FOR POTENTIAL CUSTOMERS.

AND I ALSO WANT -- JUST ONE OTHER THING. THE GENOMIC CENTER IS INDEPENDENT FROM THIS IPSC BANK.

DR. JUELSGAARD: PAT, THIS IS STEVE. HOW WILL THE 1,000 LINES BE IDENTIFIED?

DR. OLSON: I BELIEVE THAT WILL BE IN CONSULTATION, BUT I WOULD NEED TO FIND THAT OUT FOR SURE.

DR. JUELSGAARD: AS JEFF MENTIONED, THERE'S A COMMERCIAL ENTERPRISE INVOLVED. AND I THINK ONE OF THE THINGS WE JUST NEED TO BE A LITTLE COGNIZANT OF IS THAT THEY MAKE DECISIONS POTENTIALLY BASED ON COMMERCIAL VALUATIONS WHICH MAY NOT NECESSARILY BE THE SAME ONES THAT WE WOULD MAKE DECISIONS ON.

DR. OLSON: RIGHT. NOW, WE DO HAVE -- I MEAN WE WORK VERY CLOSELY WITH CORIELL, AND THEY WILL BE THE PEOPLE WHO WILL BE -- WE WILL BE WORKING WITH THEM TO DETERMINE WHAT IS SEQUENCED.

DR. JUELSGAARD: ALL RIGHT. THANKS.

MS. CHEUNG: OS, ARE YOU THERE?

DR. STEWARD: PUBLIC COMMENT. SO WE DO HAVE A MOTION AND A SECOND. TURN IT OVER TO MARIA.

CHAIRMAN THOMAS: WE HAVE PUBLIC COMMENT, OS.

DR. LORING: THIS IS JEANNE LORING. JEANNE LORING FROM THE SCRIPPS RESEARCH INSTITUTE. I HAVE TO DISCLOSE I AM ON CORIELL'S ADVISORY BOARD. SO I'VE BEEN WITH THEM DURING ONE OF THESE VALUE-ADDED PROPOSITIONS ABOUT DOING WHOLE GENOME SEQUENCING. I HAVE TO SAY THAT UNTIL JEFF MADE THAT SUGGESTION, IT DIDN'T OCCUR TO ME THAT WE COULD ACTUALLY TAKE THE RIGHT ROUTE HERE. THE CELLS HAVE ALREADY BEEN SNP GENOTYPED. THAT MEANS THAT THEY HAVE BEEN -- THE ENTIRE GENOME HAS BEEN ANALYZED IN A LESS DETAILED WAY THAN DNA SEQUENCING, BUT STILL SUFFICIENT TO BE ABLE TO, IN FACT, IDENTIFY THE INDIVIDUALS FROM WHICH THOSE CELLS CAME.

NOW, WHEN YOU START DOING DNA SEQUENCING, IF YOU PROVIDE THAT INFORMATION, AND THIS HAS BEEN A CONTENTIOUS ISSUE WITH CORIELL FOR A VERY LONG TIME, THE LAST SIX YEARS I'VE BEEN ON THEIR ADVISORY BOARD. YOU CAN IDENTIFY THE INDIVIDUALS BASED ON THEIR DNA SEQUENCE. AND SO CORIELL HAS NOT REALLY BOUGHT INTO THE IDEA YET OF RELEASING THAT INFORMATION. SO I THINK JEFF IS RIGHT IN SUGGESTING

THAT THIS IS THE KIND OF INVESTMENT THAT IS PREMATURE AND PERHAPS IS NOT GOING TO ADD VALUE AS WAS PERCEIVED BECAUSE THERE WILL BE ETHICAL ISSUES IN RELEASING THAT INFORMATION.

DR. STEWARD: THANK YOU. OTHER PUBLIC COMMENT?

MR. TORRES: OH, SHE WAS AN ADVOCATE?

DR. STEWARD: IF THERE'S NO MORE PUBLIC COMMENT THEN, I'LL TURN IT OVER TO MARIA FOR ROLL CALL.

MR. TORRES: WAIT. ON THIS POINT, DR. STEWARD, SO TO VOTE YES IS TO NOT SUPPORT THE STAFF RECOMMENDATION ON THE GENOMIC PROPOSAL; IS THAT CORRECT, ON THE QUEST?

MR. SHEEHY: THE MOTION IS NOT TO FUND ANY OF THE APPLICATIONS IN THIS ROUND.

MR. TORRES: SO IF YOU WANT TO SUPPORT THE APPLICATION, YOU WOULD VOTE NO.

DR. STEWARD: AND I THINK THEN WE WOULD CONSIDER AN ALTERNATIVE MOTION.

MR. TORRES: YES.

MR. SHEEHY: NO. THE MOTION I MADE WAS NOT TO FUND ANY OF THE APPLICATIONS IN THIS ROUND. SO THAT WOULD BE NONE. IF THAT PASSES -- A YES WOULD MEAN THAT WE WILL NOT FUND AN APPLICATION IN

THIS ROUND.

MR. TORRES: IF YOU SUPPORT THE APPLICATION, THEN YOU WOULD VOTE NO.

MR. SHEEHY: RIGHT.

MR. TORRES: OKAY. THANKS.

DR. STEWARD: OKAY. IF WE'RE CLEAR, MARIA.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: AYE.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: NO.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: I VOTE YES.

MS. BONNEVILLE: KATHY LAPORTE. LAUREN MILLER. ADRIANA PADILLA.

DR. PADILLA: YES.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: NO.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: I VOTE YES.

MS. BONNEVILLE: JEFF SHEEHY.

MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: NO.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
CHAIRMAN THOMAS: MARIA IS TABULATING HERE.
MS. BONNEVILLE: THE MOTION PASSES.
DR. STEWARD: JEFF, I THINK THE CHAIR GOES BACK TO YOU.
MR. SHEEHY: THANK YOU, OS. AND I THINK THAT CONCLUDES THE BUSINESS OF THE APPLICATION REVIEW SUBCOMMITTEE. SO IT'S BACK TO YOU, CHAIRMAN THOMAS, IF THERE'S ANY OTHER BUSINESS FOR THE ICOC OR TO ADJOURN.
CHAIRMAN THOMAS: THANK YOU, MR. SHEEHY. WE HAVE NOW REACHED THE GENERAL PUBLIC COMMENT PORTION OF THE AGENDA. ARE THERE ANY MEMBERS OF THE PUBLIC EITHER HERE OR AT OTHER LOCATIONS THAT WOULD LIKE TO COMMENT ON WHATEVER IS ON THEIR MIND? YES, SIR.

DR. LAIKIND: HI. I'M PAUL LAIKIND. I'M PRESIDENT AND CEO OF VIACYTE, AND I WANTED TO READ A PREPARED REMARKS INTO THE RECORD.

I WANT TO TAKE THIS OPPORTUNITY TO THANK CIRM FOR THE IMPORTANT WORK THAT THEY ARE DOING TO PROMOTE THE PROMISING FIELD OF REGENERATIVE MEDICINE ON BEHALF OF ALL THE CITIZENS OF CALIFORNIA. AT VIACYTE WE ARE HONORED TO HAVE PARTNERED WITH CIRM TEAM TO DEVELOP STEM CELL-DERIVED THERAPIES WITH THE POTENTIAL TO TRANSFORM THE LIVES OF PATIENTS WITH DIABETES. THE FINANCIAL TECHNICAL SUPPORT PROVIDED BY CIRM HAS ALLOWED US TO ADVANCE THE FIRST EVER ALLOGENEIC ENCAPSULATED CELL THERAPY PRODUCT INTO THE CLINIC. THIS IS CALLED VC-01 WHICH WE'RE NOW CALLING PEC-ENCAP.

I CAN'T OVER EMPHASIZE THE IMPORTANCE OF THE CLINICAL WORK WE'RE DOING WITH PEC-ENCAP. NOT ONLY ARE WE GAINING INSIGHTS TO MAKE THIS PRODUCT CANDIDATE SUCCESSFUL, WE'RE ALSO ADVANCING THE FIELD IN GENERAL. WHEN MY FRIENDS ASK ME HOW THINGS ARE GOING AT VIACYTE, I OFTEN SAY THAT CHANGING THE WORLD IS NOT EASY AND IT'S NOT. SO WITH THE HELP OF CIRM AND AS WELL HELP FROM OUR FRIENDS AT JDRF, WE'RE MAKING STEADY PROGRESS WITH THE PEC-ENCAP TOWARDS AN IMPORTANT NEW TREATMENT FOR THE MAJORITY

OF PATIENTS WITH INSULIN-DEPENDENT DIABETES.

BUILDING ON WHAT WE HAVE LEARNED THUS FAR WITH PEC-ENCAP, WE ARE NOW APPROACHING THE CLINIC WITH THE SECOND RELATED PRODUCT CANDIDATE WHICH THE COMMITTEE -- THE BOARD VOTED ON THIS MORNING. THIS PRODUCT CANDIDATE CALLED PEC-DIRECT IS BEING DEVELOPED FOR A SUBSET OF PATIENTS WITH DIABETES THAT ARE AT VERY HIGH RISK FOR ACUTE COMPLICATIONS. THESE HIGH RISK PATIENTS SUFFER SOME SEVERE HYPOGLYCEMIC EPISODES, EXTREME GLYCEMIC LABILITY, IMPAIRED AWARENESS OF HYPOGLYCEMIA, AND ARE AT CONSTANT RISK OF HOSPITALIZATION, EVEN DEATH.

IN THE U.S. ALONE IT'S ESTIMATED THAT OVER 125,000 TYPE 1 DIABETIC PATIENTS ARE IN THIS HIGH RISK CATEGORY. THE PATIENT POPULATION BEING TARGETED WITH PEC-DIRECT, WHICH WAS VOTED ON THIS MORNING AND APPROVED, IS GENERALLY THE SAME POPULATION THAT WOULD BE ELIGIBLE FOR CADAVER ISLET TRANSPLANTS, A PROCEDURE THAT CAN BE HIGHLY EFFECTIVE, BUT SUFFERS FROM A SEVERE LACK OF DONOR MATERIAL AS WELL AS OTHER LIMITATIONS.

WE BELIEVE PEC-DIRECT CAN OVERCOME THE LIMITATIONS OF CADAVER ISLET TRANSPLANTS BY PROVIDING AN UNLIMITED SUPPLY OF CELLS DERIVED FROM EMBRYONIC STEM CELL STARTING MATERIAL MANUFACTURED

UNDER CGMP CONDITIONS AND A SAFER, MORE OPTIMAL ROUTE OF ADMINISTRATION. MOREOVER, BASED ON THE CLINICAL STUDIES AND INFORMED BY WHAT WE HAVE LEARNED WITH THE PEC-ENCAP, WE BELIEVE THAT PEC-DIRECT HAS A GOOD PROBABILITY OF RELATIVELY RAPID ADVANCEMENT AND SUCCESS IN THE CLINIC.

THE WORK WE ARE DOING ON PEC-DIRECT AND PEC-ENCAP REPRESENTS HOPE TO MILLIONS OF DIABETES PATIENTS, NOT JUST IN CALIFORNIA, BUT WORLDWIDE. THE AMAZING PROGRESS MADE TO DATE ON THESE PROJECTS AND MANY OTHERS IN THE REGENERATIVE MEDICINE SPACE WOULD NOT HAVE BEEN POSSIBLE WITHOUT THE STRONG SUPPORT OF CIRM. SO I REALLY WANT TO AGAIN THANK YOU FOR THE IMPORTANT WORK THAT EVERYONE AT CIRM AND ON THE BOARD ARE DOING.

CHAIRMAN THOMAS: THANK YOU VERY MUCH, PAUL, FOR YOUR COMMENTS. ANY OTHER PUBLIC COMMENTS? YES. WE HAVE ONE PUBLIC -- AT LEAST ONE MORE HERE.

UNIDENTIFIED SPEAKER: THANK YOU, ICOC MEMBERS AND CIRM BOARD FOR ALL YOUR HARD WORK ON BEHALF OF TYPE 1 DIABETICS LIKE ME AND OTHERS. I WANT TO THANK IN PARTICULAR JEFF AND YOU, JONATHAN, AND ART AND FRANCISCO. YOU FOLKS KNOW ME AND KNOW MY WIFE WELL. LORRAINE IS NOT HERE TODAY. SHE IS IN WASHINGTON, D.C. TESTIFYING BEFORE THE FOOD AND

DRUG ADMINISTRATION ABOUT DEXCOM AND THE USES OF DEXCOM IN TYPE 1 DIABETES. SO OTHERWISE SHE WOULD BE HERE. AND SHE WANTS ME TO THANK YOU ON HER BEHALF AS WELL.

THIS VIACYTE WORK IS EXTREMELY IMPORTANT TO ME AS YOU CAN IMAGINE. I'VE HAD TYPE 1 FOR 57 YEARS. THAT'S QUITE A WHILE. THERE ARE ONLY 3,000 OF US ESTIMATED THAT HAVE HAD DIABETES MORE THAN 50 YEARS IN THE U.S., AND WE ALL MEET AT THE JOSLIN DIABETES CENTER IN BOSTON EVERY TWO YEARS, VERY EXCITING EVENT. AND I BELIEVE, BECAUSE OF THE WORK OF CIRM AND JDRF AND OTHERS, THAT I WILL BE CURED IN MY LIFETIME, AND THAT EXCITES ME QUITE A BIT. I WAS DIAGNOSED IN 1959, '60. I DIDN'T THINK THAT WOULD EVER HAPPEN. PEOPLE TOLD ME IT WAS NOT POSSIBLE, BUT THANKS TO YOU AND YOUR WORK, IT IS POSSIBLE, I BELIEVE. SO THANK YOU VERY MUCH FOR THAT.

AND THE OTHER ASPECT OF THE VIACYTE WORK PARTICULARLY THAT WAS MENTIONED WAS THAT THEY MIGHT HAVE APPLICATION TO TYPE 2. FOR THE LAST YEAR AND A HALF, LORRAINE AND I HAVE BEEN WORKING IN SUPPORT OF THE CDC REVAMPING DIABETES EDUCATION FOR TYPE 2 PATIENTS AS WELL. AND THAT'S PRETTY EXCITING FOR THOSE FOLKS.

SO, JONATHAN, YOU TALKED EARLIER ABOUT

CO-FUNDING WITH OTHER ORGANIZATIONS. AS YOU KNOW, JDRF IS FUNDING SOME OF THE VIACYTE WORK. I THINK ADA AND OTHER ORGANIZATIONS ARE POSSIBILITIES FOR THIS CURRENT WORK THAT THEY'RE TALKING ABOUT BECAUSE THAT WILL AFFECT TYPE 2S AS WELL, AND THAT'S A MUCH BIGGER ISSUE, AS I'M SURE YOU'RE AWARE. NINETY PERCENT OF THE DIABETICS IN THIS COUNTRY ARE TYPE 2.

I HAVE HAD TWO STROKES AND TWO BRAIN SURGERIES SINCE I LAST SAW YOU ALL, SO FORGIVE ME IF MY SPEECH IS NOT PERFECT, BUT I'M DOING THE BEST I CAN THROUGH THERAPY TO IMPROVE. SO THANK YOU VERY MUCH FOR ALL THE WORK YOU DO AND FOR YOUR SUPPORT SINCE 2004 WHEN LORRAINE AND I FIRST STARTED WORKING ON PROP 71. AND THANKS TO VIACYTE FOR THE WORK THEY DO, AND THANK YOU FOR FUNDING THEM. APPRECIATE IT VERY MUCH.

CHAIRMAN THOMAS: THANK YOU, CHRIS, AND THANK YOU FOR ALL YOUR PAST WORK, YOU AND LORRAINE, ON BEHALF OF CIRM AND PATIENTS. THANK YOU. ANY OTHER PUBLIC COMMENT?

MS. CHEUNG: NO PUBLIC COMMENT IN OAKLAND. THIS IS JUST A REMINDER TO THE BOARD MEMBERS THAT THE NEXT TELEPHONIC MEETING WILL BE ON AUGUST 25TH, AND OUR NEXT IN-PERSON MEETING WILL BE SEPTEMBER 21ST, AND I WILL SEND ADDITIONAL DETAILS IN THE NEXT

COUPLE OF WEEKS.

CHAIRMAN THOMAS: THANK YOU. HEARING NO FURTHER PUBLIC COMMENT, THAT BRINGS US TO THE END OF THE AGENDA. THANK YOU ALL FOR ATTENDING AT THE VARIOUS SITES AND FOR ALL THE BOARD MEMBERS AND TEAM, ANOTHER EXCELLENT MEETING, AND WE STAND ADJOURNED.

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 TELEPHONIC PROCEEDINGS BEFORE THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE AND THE APPLICATION REVIEW SUBCOMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON JULY 21, 2016, 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.

BETH C. DRAIN, CSR 7152
BARRISTERS' REPORTING SERVICE
160 S. OLD SPRINGS ROAD
SUITE 270
ANAHEIM, CALIFORNIA
(714) 444-4100