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 MEETING

LOCATION: AS INDICATED ON THE AGENDA

DATE: THURSDAY, FEBRUARY 18, 2016
11 A.M.

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

BRS FILE NO.: 98345

I N D E X

THURSDAY, FEBRUARY 18, 2016

11 A.M.

CHAIRMAN THOMAS: GOOD MORNING, EVERYBODY. WELCOME TO THIS RENDITION OF THE APPLICATION REVIEW SUBCOMMITTEE. MARIA, WILL YOU PLEASE CALL THE ROLL.

MS. BONNEVILLE: SURE.

DAVID BRENNER. LINDA BOXER. KEN BURTIS. ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: LEON FINE. MICHAEL FRIEDMAN. JUDY GASSON. SAM HAWGOOD. DAVID HIGGINS.

DR. HIGGINS: HERE.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: HERE.

MS. BONNEVILLE: SHERRY LANSING. KATHY LAPORTE.

MS. LAPORTE: HERE.

MS. BONNEVILLE: BERT LUBIN. SHLOMO MELMED. LAUREN MILLER.

MS. MILLER: HERE.

MS. BONNEVILLE: ADRIANA PADILLA.

DR. PADILLA: HERE.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: HERE.

MS. BONNEVILLE: ROBERT PRICE. FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. BONNEVILLE: CARMEN PULIAFITO. ROBERT QUINT. AL ROWLETT. JEFF SHEEHY.

MR. SHEEHY: HERE.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: HERE.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: HERE.

MS. BONNEVILLE: ART TORRES. KRISTINA VUORI. DIANE WINOKUR.

MR. ROWLETT: AL ROWLETT JUST JOINED.

MS. BONNEVILLE: THANK YOU, AL.

CHAIRMAN THOMAS: GOOD MORNING, AL.

SO WE HAVE ONE ITEM FOR CONSIDERATION TODAY WHICH IS CONSIDERATION OF APPLICATIONS SUBMITTED IN RESPONSE TO CLIN1: PARTNERING OPPORTUNITY FOR LATE STAGE PRECLINICAL PROJECTS. WE HAVE ONE TO BE DISCUSSED TODAY. WE'LL TURN IT OVER TO DR. SAMBRANO.

DR. SAMBRANO: THANK YOU, J.T. GOOD MORNING, EVERYBODY. I'M JUST GOING TO PROVIDE AN OVERVIEW FOR THIS PROGRAM AND WHAT THE

RECOMMENDATIONS FROM THE GRANTS WORKING GROUP ARE REGARDING THIS APPLICATION.

SO JUST A REMINDER ABOUT THE CLINICAL STAGE PROGRAM WHICH ACCEPTS AND SUPPORTS APPLICATIONS FOR PROJECTS THAT ARE AT VARIOUS STAGES ALONG THE CLINICAL PIPELINE FROM IND-ENABLING THROUGH CLINICAL TRIAL. THIS PARTICULAR PROJECT IS A CLIN1 APPLICATION IN WHICH THEY ARE SEEKING TO DO IND-ENABLING WORK TO READY THEM FOR A CLINICAL TRIAL.

A REMINDER OF THE SCORING SYSTEM THAT WE UTILIZE FOR THIS CLINICAL PROGRAM, WHICH IS A SCORE 1, 2, OR 3. A SCORE OF 1 MEANS THAT THE GRANTS WORKING GROUP FELT THE APPLICATION HAD EXCEPTIONAL MERIT AND WARRANTS FUNDING. A SCORE OF 2 MEANS THAT IT NEEDS IMPROVEMENT AND DOES NOT WARRANT FUNDING AT THIS TIME, BUT THEN COULD BE RESUBMITTED TO ADDRESS THE PROBLEM AREAS. AND A SCORE OF 3 WHICH MEANS THAT IT IS SUFFICIENTLY FLAWED THAT IT DOES NOT WARRANT FUNDING AT THIS TIME AND SHOULD NOT BE RESUBMITTED.

THIS SPECIFIC PROGRAM, CLIN1-08342, IS A DEVELOPMENT PROGRAM FOR A PRODUCT INTENDED TO IMPROVE CORD BLOOD TRANSPLANT OUTCOMES. THEIR PRODUCT IS CALLED AB-110, AND WHAT IT IS, IT'S A

CD34+ CORD BLOOD-DERIVED HEMATOPOIETIC STEM CELL AND PROGENITOR CELL THAT ARE CO-CULTURED AND THEY ARE CO-INFUSED WITH GENETICALLY MODIFIED ENDOTHELIAL CELLS. SO THIS COMBINATION OF CELL PRODUCT IS INTENDED TO HELP PATIENTS THAT HAVE LIFE-THREATENING, HIGH RISK HEMATOLOGIC MALIGNANCIES SUCH AS LEUKEMIA AND LYMPHOMA. AND, OF COURSE, THE GOAL OF THEIR PROJECT IS TO COMPLETE ALL THE PRECLINICAL RESEARCH ACTIVITIES TO GET TO AN IND SUBMISSION AND COMMENCE A PHASE I TRIAL.

SPECIFIC ACTIVITIES ARE TO DEVELOP AND VALIDATE THEIR GMP PROCESS, TO MANUFACTURE THIS COMPLEX PRODUCT IN A CLOSED BIOREACTOR SYSTEM, TO COMPLETE THE SAFETY ASSESSMENT OF THEIR ENDOTHELIAL CELL COMPONENT, AND TO PREPARE AND FILE AN IND APPLICATION WITH THE FDA TO BEGIN THEIR STUDIES.

THE AMOUNT OF FUNDS REQUESTED ARE ABOUT 3.8 MILLION AND PROVIDE CO-FUNDING AT 20 PERCENT. I WANT TO MAKE A NOTE ABOUT THE FUNDS REQUESTED. FOLLOWING THE GWG REVIEW, WE WORKED WITH THIS GROUP IN ORDER TO INCREASE THE AMOUNT OF FUNDING THAT IS BEING REQUESTED BY 400,000. THIS IS IN RESPONSE TO SPECIFIC COMMENTS MADE BY THE GRANTS WORKING GROUP RELATED TO THE COMPARABILITY OF THEIR BIOREACTOR SYSTEM VERSUS WHAT THEY HAD PREVIOUSLY PROPOSED,

WHICH THESE WERE STUDIES THAT THEY FELT WOULD BE IMPORTANT TO DO. AND WITH THE ADDITION OF MORE TIME TO ACCOMPLISH THESE, IT REQUIRED 400,000 ADDITIONAL DOLLARS. SO THAT'S INCLUDED IN THE AMOUNT THAT WE ARE NOTING THERE FOR THE AMOUNT REQUESTED.

AS WITH ALL PROJECTS, THEY UNDERGO AN INITIAL BUDGET REVIEW, WHICH THIS APPLICATION, OF COURSE, PASSED, TO GET TO THE GRANTS WORKING GROUP. THE GRANTS WORKING GROUP GAVE IT A SCORE OF 1 WITH EIGHT VOTES SCORING IN THE 1 RANGE AND FOUR INDIVIDUALS SCORING IT AT 2, AND NO ONE SCORING THIS A 3.

THE CIRM TEAM ALSO REVIEWS THESE RECOMMENDATIONS FROM THE GRANTS WORKING GROUP. WE CONCUR WITH THE GRANTS WORKING GROUP RECOMMENDATION TO FUND THIS PROJECT. AND, OF COURSE, OF NOTE, THIS WAS A PROJECT THAT WAS SUBMITTED BACK IN SUMMER LAST YEAR. AND UNDER THE ORIGINAL REVIEW, IT RECEIVED A 2. SO THEY TOOK A FEW MONTHS TO REVISE THEIR PROJECT AND PROVIDE A NEW PROPOSAL WHICH WAS WELL RECEIVED BY THE GRANTS WORKING GROUP PANEL, WHICH, IF YOU LOOK TO THE SUMMARY, HAS A LOT TO DO WITH THE REASON THEY FELT THIS NOW MERITS FUNDING. AND SO THEIR NEW SCORE IS A 1 REFLECTING ALL THE CHANGES THAT WERE MADE OVER THIS TIME.

SO THAT'S ALL I HAVE. AND IF YOU HAVE QUESTIONS, HAPPY TO ADDRESS THEM.

CHAIRMAN THOMAS: THANK YOU, DR. SAMBRANO, FOR THE DISCUSSION ON THE PROPOSAL. I TURN THE MEETING NOW OVER TO MR. SHEEHY.

MR. SHEEHY: THANK YOU, J.T. SO IN ORDER TO START, I THINK IF SOMEONE WOULD LIKE TO MAKE EITHER A MOTION TO ACCEPT THE GRANTS WORKING GROUP'S RECOMMENDATION TO FUND THIS PROJECT OR TO REJECT THE RECOMMENDATION AND NOT FUND IT.

DR. DULIEGE: I'M HAPPY TO MAKE A MOTION.

MR. SHEEHY: TO FUND?

DR. DULIEGE: YES.

MR. SHEEHY: THANK YOU, ANNE-MARIE. IS THERE A SECOND?

DR. HIGGINS: YES, A SECOND.

MR. SHEEHY: GREAT. ANY DISCUSSION?

MR. PANETTA: JEFF, THIS IS JOE PANETTA. MAY I ASK A QUESTION?

MR. SHEEHY: SURE, PLEASE.

MR. PANETTA: I'M IN FAVOR -- WELL, WE'LL GET TO THE VOTE. BUT I'M A LITTLE UNCLEAR AS TO THE DEGREE TO WHICH THE MANUFACTURING PROCESS IS A CONCERN WITHIN THIS APPLICATION OR IF THIS IS SOMETHING THAT WILL NEED TO BEGIN TO BE DEALT WITH

WITHIN THIS GRANT AND THEN WORKED ON FINALLY LATER ON? BECAUSE IN READING THROUGH THE SUMMARY, I HAD THE IMPRESSION THAT THERE ARE STILL CONCERNS ABOUT THE RIGOR OF THE MANUFACTURING PROCESS.

DR. SAMBRANO: YES. SO THERE WERE CONCERNS WITH THE ORIGINAL --

MS. WINOKUR: EXCUSE ME. THIS IS DIANE.

DR. SAMBRANO: THANKS FOR JOINING US.

SO THERE WERE CONCERNS WITH THE ORIGINAL SUBMISSION REGARDING THE MANUFACTURING PROCESS GIVEN THE COMPLEX NATURE OF THIS PRODUCT. AND SO THE APPLICANTS HAVE ADDRESSED THAT IN PART BY PROPOSING NOW A CLOSED BIOREACTOR SYSTEM TO MANUFACTURE THIS PRODUCT. BUT, YES, THERE ARE STILL SOME CONCERNS ABOUT DEMONSTRATING COMPARABILITY WITH THEIR ORIGINAL PROCESS TO SHOW THAT THEY CAN ATTAIN A SIMILAR EFFICACY IN MODELS WITH THE PRODUCT MANUFACTURED IN THIS WAY. SO PART OF IT IS THAT.

THE OTHER IS CONTINUING TO DEVELOP A PROCESS THAT'S GOING TO BE COST-EFFECTIVE AS THEY MOVE FORWARD. HOWEVER, THE GRANTS WORKING GROUP FELT THAT THESE ARE ELEMENTS THAT ARE FIXABLE. AND AS THEY MOVE FORWARD IN THE DEVELOPMENT PIPELINE, THAT WORKING TOGETHER WITH CIRM, THESE ARE RESOLVABLE, AND THEY FELT COMFORTABLE THAT THIS WAS

SOMETHING THAT THEY FELT SHOULD BE FUNDED WITH THE CAVEAT THAT THEY WOULD BE WORKING CLOSELY WITH CIRM TO ADDRESS ISSUES.

MR. PANETTA: OH, GREAT. OKAY. THAT ANSWERS MY QUESTION. THANK YOU.

MR. SHEEHY: ARE THERE ADDITIONAL --

DR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD. YES, I DID HAVE SOME ADDITIONAL QUESTIONS. THEY SORT OF LIE IN TWO DIFFERENT AREAS.

SO, FIRST, I WANT TO FOLLOW UP ON THE QUESTION THAT JOE JUST RAISED, BUT LOOK AT IT A LITTLE DIFFERENTLY. SO IF YOU LOOK AT, NOT AT THE PRESENTATION, BUT AT THE CLINICAL PROJECT, THE REVIEW THAT THE GWG GAVE, AT THE VERY END OF THAT UNDER IS THE PROJECT FEASIBLE AND THEN SUB-C. AND IT SAYS, "IT IS NOT CLEAR THAT THE TEAM FULLY UNDERSTAND THE SIGNIFICANCE OF SWITCHING TO A NEW BIOREACTOR PLATFORM AND THE NEED TO REPEAT MUCH OF THE PREVIOUS NONBIOREACTOR EXPERIMENTAL TEST RESULTS IN ORDER TO SHOW COMPARABILITY. THIS IS NOT ACCOUNTED FOR IN THE CURRENT PROJECT PLAN OR IN THE CONTINGENCY PLAN."

SO I JUST WANT TO -- FOR ME THAT'S AN IMPORTANT CRITICISM BECAUSE WHAT THEY'RE DOING IS THEY'RE GOING TO A WHOLLY DIFFERENT PROCESS THAN THE

ONE THAT THEY HAVE BEEN USING. NOW THEY USE A BIOREACTOR INSTEAD OF WHATEVER THE PREVIOUS PROCESS IS. AND SO AT THE END OF THE DAY, WHEN YOU'RE DEALING WITH BIOLOGICS, BIOLOGICS ARE THE OUTCOME OF A PROCESS. AND SO THE PROCESS MAKES A DIFFERENCE. SO THIS QUESTION, DR. SAMBRANO, IS REALLY RELATED TO OUR PLANS FOR MONITORING WHAT THEY'RE DOING AND PUTTING IN STOPPING POINTS ALONG THE WAY IF THEY SEEM TO BE REACHING DEADENDS OR DIFFICULTIES. THIS IS NOT A SIMPLE THING IN MY MIND, THIS CHANGEOVER TO A WHOLLY DIFFERENT PROCESS. AND I THINK WE NEED TO REALLY, IN MY MIND, STAY ON TOP OF IT; AND IF THIS DOESN'T SEEM TO BE HEADED IN THE RIGHT DIRECTION, WE NEED TO BE ABLE TO PUT THE BRAKES ON WHETHER TO SLOW IT DOWN OR TO STOP IT COMPLETELY.

IN ADDITION TO THAT, I THEN ALSO SEE IN THESE COMMENTS THAT THEY SAY THEY'RE HEAVILY RELIANT ON A SINGLE INDIVIDUAL -- THIS IS ACTUALLY IN B JUST BEFORE THAT -- TO DEVELOP THEIR MANUFACTURING PROCESS. SO THERE'S ALWAYS A RISK WHEN YOU'RE DOWN TO KIND OF ONE PERSON WHO IS THE PERSON YOU'RE REALLY LEANING ON ON ALL OF THIS. AND, AGAIN, IF SOMETHING WERE TO HAPPEN TO THAT INDIVIDUAL, THEY WERE TO LEAVE OR THEY WERE TO BECOME INCAPACITATED OR WHATEVER, AND AGAIN, WE NEED TO BE ABLE, AT LEAST

IN MY MIND, TO THROTTLE THIS BACK A LITTLE BIT.

SO IF YOU CAN RESPOND TO THOSE THINGS, I WOULD APPRECIATE IT.

DR. SAMBRANO: SURE. AND, YES, YOU'RE ABSOLUTELY RIGHT. THESE WERE CONCERNS FROM THE GRANTS WORKING GROUP. THAT IS ALSO THE REASON WHY WE FELT COMPELLED, BEFORE BRINGING THIS PROJECT TO YOU, THAT WE TRY TO BEGIN WORKING WITH THEM AND ADDRESS THESE ISSUES.

SO I MENTIONED THAT THE AMOUNT REQUESTED HAS INCREASED A BIT, AND PART OF IT WAS TO NOW INCLUDE THOSE COMPARABILITY STUDIES THAT THE GRANTS WORKING GROUP WAS CONCERNED ABOUT WITHIN THIS PLAN AND TO ALSO SET MILESTONES THAT CLEARLY DELINEATE THE ACCOMPLISHMENT OF THOSE ACTIVITIES AND SET A PLAN FOR THEM TO GO FORWARD.

SO THOSE HAVE BEEN TAKEN INTO ACCOUNT BECAUSE OF THE CONCERNS OF THE GRANTS WORKING GROUP, AND SO WE HAVE ALREADY BEGUN TO WORK WITH THEM IN ORDER TO REMEDY AND ADDRESS THEM.

DR. MILLS: SO THE SECOND THING IS UNDER, GENERALLY SPEAKING, YOUR CONCERNS THROUGHOUT HERE ARE, BUT THIS IS A PRECLINICAL STAGE AND IND-ENABLING PHASE OF WORK. SO CLEARLY SOME OF THESE THINGS THAT ARE BEING DONE NEED TO BE DONE IN

ORDER TO GET TO THE IND AND THERE'S INHERENT RISK ABOUT THAT. BUT, IN GENERAL, THE APPROACH TO EVERYTHING WE DO UNDER 2.0 IS NOW MILESTONE BASED. SO IF THEY DON'T ACCOMPLISH MILESTONE A, THERE IS NO MILESTONE B. SO THE PROCESS ITSELF TAKES CARE OF A LOT OF YOUR CONCERNS.

DR. JUELSGAARD: JUST SPEAKING TO THAT, RANDY, REAL QUICKLY, SO I PICK UP ON THE POINT THAT THEY MADE, WHICH IS THAT THEY'RE HIGHLY DEPENDENT ON A SINGLE INDIVIDUAL FOR THE MANUFACTURING PROCESS. MANUFACTURING A PARTICULAR PROCESS DEVELOPMENT IS A SPECIALIZED AREA. SO WHEN WE HAVE SOMEBODY ON OUR SIDE LOOKING OVER THEIR SHOULDER AT WHAT THEY'RE DOING, IS THAT SOMEBODY INTERNALLY OR EXTERNALLY THAT'S JUDGING THAT WE'RE HEADED OR THEY'RE HEADED IN THE RIGHT DIRECTION WITH REDOING THIS USING A BIOREACTOR APPROACH? SO WHAT'S THE EXPERTISE THAT WE RELY ON TO MAKE SURE THAT WE THINK THEY'RE MAKING PROGRESS?

DR. MILLS: BECAUSE THIS WOULD BE A CLINICAL STAGE PROGRAM, IT WOULD EVENTUALLY HAVE A CAP, A CLINICAL ADVISORY PANEL, AND THAT WILL INCLUDE INTERNAL EXPERTS, EXTERNAL EXPERTS, AND AT LEAST ONE PATIENT ADVOCATE. AND THAT GROUP MEETS QUARTERLY TO LOOK AT WHAT THEY'RE DOING AND GO OVER

THESE ISSUES AND HELP WHERE NEED BE.

DR. JUELSGAARD: SO THE SHORT ANSWER TO MY QUESTION IS THAT WE DO HAVE SOMEBODY WITH PROCESS EXPERIENCE THAT WILL BE INVOLVED IN THIS FROM EARLY ON, AND WE'LL BASICALLY BE GETTING FEEDBACK ON HOW THIS CHANGEOVER TO A BIOREACTOR PROCESS IS WORKING?

DR. MILLS: YEAH. THE WAY WE FORMULATE THE CAP, STEVE, IS THAT WE LOOK AT THE PROJECT AND WE LOOK AT ITS OVERALL NEEDS. AND SO BASICALLY WHAT ARE THE THINGS DURING THIS PROJECT'S LIFE THAT ARE GOING TO BE MOST LIKELY TO KEEP IT FROM BEING SUCCESSFUL? AND THEN WE POPULATE THAT CAP WITH INDIVIDUALS THAT ALIGN MOST CLOSELY AND BEST TO BE ABLE TO MITIGATE THOSE RISKS AND GIVE IT THE BEST CHANCE FOR SUCCESS. THAT MAKE SENSE?

DR. JUELSGAARD: YES. AGAIN, I THINK IT'S HAVING THE RIGHT PEOPLE WITH THE RIGHT EXPERTISE LOOKING OVER THEIR SHOULDER. THAT'S KIND OF THE POINT I WAS MAKING. I DON'T KNOW IF THERE ARE ANY OTHER QUESTIONS ABOUT THE MANUFACTURING PROCESS. IF THERE ARE, I'LL STOP FOR A MOMENT, BUT I'VE GOT AN ADDITIONAL QUESTION THAT REALLY GOES TO MECHANISM OF ACTION.

MS. WINOKUR: THIS IS DIANE. I HAVE SOME COMMENTS ON THE DISCUSSION. I HAVE THE SAME

CONCERNS, AND I ENDED UP WITH AN OVERALL FEELING ABOUT THIS PROPOSAL THAT WE ARE, IN ESSENCE, WRITING THIS FOR THEM.

DR. MILLS: DID YOU SAY WRITING?

MS. WINOKUR: YEAH. WE ARE TELLING THEM WHAT TO PUT IN THE PROPOSAL, THE BIOREACTOR COMPARABILITY ISSUE, THE ONLY ONE PERSON ISSUE, SEVERAL OTHERS THAT WE ARE GOING TO BE LOOKING AT, EVALUATING AS THEY GO ALONG.

DR. MILLS: SO, AGAIN, UNDER SORT OF THE NEW CIRM 2.0 CONCEPT, AND PARTICULARLY THE WAY THE NEW SCORING SYSTEM WORKS, WHAT WE'VE DONE IS WE TAKE AS AN AGENCY A FAR MORE ACTIVE APPROACH. AND SO WE DON'T -- JUST TO BE CLEAR BECAUSE JAMES WILL WANT ME TO BE CLEAR ON THIS, UNDER NO CIRCUMSTANCES DO WE WRITE THEIR APPLICATION FOR THEM. BUT WHEN WE DO THE REVIEW PROCESS, AND THIS WAS A GREAT EXAMPLE, THIS APPLICATION ON ITS FIRST REVIEW RECEIVED A SCORE OF A 2, AND THERE WERE TWELVE 2 VOTES ON THIS APPLICATION. AND WE ASKED THE EXPERTS OF THE GWG TO TELL US WHY THEY GAVE IT A 2 AND WHAT THEY WANTED TO SEE THAT WAS DIFFERENT AND HOW CAN WE MAKE THE APPLICATION BETTER.

AND SO THAT'S WHAT HAPPENED HERE. WE SENT BACK PRETTY COMPREHENSIVE COMMENTS. I'LL SAY A LOT

OF TIMES WHEN WE GIVE SOMEBODY A 2, WE WILL OFTEN GET A TURNAROUND OF THAT DOCUMENT IN A VERY SHORT PERIOD OF TIME, SOMETIMES WITHIN SEVEN DAYS OR TEN DAYS OR SOMETHING LIKE THAT, BUT IN THIS CASE THEY ACTUALLY TOOK THESE COMMENTS TO HEART. AND IT TOOK THEM A CONSIDERABLE AMOUNT OF TIME, SEVERAL MONTHS, SIX MONTHS, TO ACTUALLY GO BACK AND THINK THROUGH ALL THE COMMENTS AND THINK ABOUT HOW THEY WANTED TO MODIFY THEIR PLAN.

AND THE RESULT THAT CAME BACK ACTUALLY I THINK IS EXACTLY WHAT THE 1, 2, 3 SCORING SYSTEM WAS INTENDED TO DO. IT WAS INTENDED TO TAKE THE BEST ADVICE FROM THESE EXPERT REVIEWERS AND USE IT TO MAKE A MARGINAL APPLICATION MUCH STRONGER. AND THEY DID THAT HERE. AND THE GWG WAS ALSO CLEAR THAT, WHILE THIS APPLICATION WAS NOW CLEARLY IN THE FUNDABLE RANGE, THERE WERE OTHER THINGS THAT COULD BE DONE TO MAKE IT EVEN STRONGER THAN THAT. AND THAT GOES TO STEVE'S COMMENT WITH REGARDS TO THE BIOREACTOR AND THE GWG SORT OF RECOMMENDATIONS THAT WEREN'T TRANSFORMING THE APPLICATION ANYMORE, BUT INSTEAD OF SORT OF MORE AT THE HIGHER END OF POLISHING IT TO GIVE IT A GREATER CHANCE TO SUCCEED.

AND SO THAT'S HOW THIS PROCESS WORKS. I ACTUALLY CONSIDER THE FEEDBACK CONSIDERATION AND

REAPPLICATION THAT TOOK PLACE HERE A REALLY GREAT EXAMPLE OF HOW THE NEW SCORING SYSTEM SHOULD WORK.

MS. WINOKUR: DID IT AFFECT THE BUDGET?

DR. MILLS: IT AFFECTED THE BUDGET TO THE TUNE OF ABOUT $400,000 ON THE UPSIDE.

MR. SHEEHY: ARE THERE ADDITIONAL COMMENTS ON THIS PARTICULAR ISSUE ABOUT MANUFACTURING? I THINK STEVE HAS SOME OTHER QUESTIONS/COMMENTS THAT HE WANTED TO BRING IN. BUT ON THIS ONE ISSUE, THE MANUFACTURING, IS THERE ANYTHING ELSE? OKAY. STEVE.

DR. JUELSGAARD: SO THIS PRODUCT, WHICH IS A COMBINATION PRODUCT, TWO DIFFERENT CELL TYPES, IS DESIGNED TO TREAT HEMATOLOGICAL MALIGNANCIES, IN PARTICULAR LEUKEMIA AND LYMPHOMAS, GENERALLY SPEAKING. AND SO ONE OF THE WAYS THAT'S DONE CURRENTLY IS WITH BONE MARROW TRANSPLANTATION, RIGHT? SO, DR. SAMBRANO, CAN YOU JUST -- AND THIS IS MORE A MATTER OF CURIOSITY THAN CRITICISM, BUT CAN YOU DESCRIBE THE MECHANISM OF ACTION? HOW ARE THEY HOPING TO ACHIEVE THE TREATMENT OF HEMATOLOGICAL MALIGNANCIES USING CD34+ CORD-DERIVED HEMATOPOIETIC CELLS COMBINED WITH GENETICALLY MODIFIED ENDOTHELIAL CELLS?

SO I'M NOT QUITE SURE I UNDERSTAND THE

SCIENTIFIC BASIS FOR THIS, AND I'M JUST CURIOUS ABOUT THAT.

DR. SAMBRANO: I CAN SPEAK TO IT ONLY TO SOME EXTENT. WHAT THEY ARGUE IS THAT THE ENDOTHELIAL CELL COMPONENT PROVIDES MORE OF THE NATIVE ENVIRONMENT FOR THE HEMATOPOIETIC AND PROGENITOR CELLS IN ORDER TO EXPAND, SO IT ENHANCES THEIR ABILITY TO EXPAND AND ALSO TO ENGRAFT. AND SO BY HAVING THE CELL COMBINATION, IT IMPROVES ON THE ABILITY OF THE HSC'S TO ENGRAFT AND ENGRAFT MORE RAPIDLY.

MR. SHEEHY: STEVE, COULD I ACTUALLY ADD TO THAT BECAUSE I ACTUALLY LOOKED AT THIS REALLY CLOSELY?

DR. JUELSGAARD: SURE.

MR. SHEEHY: SO THIS IS ONE OF THE HOLY GRAILS IN THE HEMATOPOIETIC STEM CELL RESEARCH, WHICH IS THE ABILITY TO EXPAND THE POPULATION EX VIVO. AND SO WHAT THEY'RE BASICALLY TRYING TO DO IS RECAPITULATE THE HEMATOPOIETIC STEM CELL NICHE SO THAT YOU CAN GET, LIKE IF YOU DO AN AUTOLOGOUS TRANSPLANT, YOU CAN GET THE CELLS OUT OF SOMEONE AND GREATLY EXPAND THEM OR THESE CORD BLOOD UNITS CAN BE GREATLY EXPANDED. SO WHERE YOU'RE USING TWO CORD BLOODS, YOU CAN ACTUALLY GET BY WITH USING ONE.

SO PEOPLE ARE EXPERIMENTING WITH CHEMICAL AGENTS TO TRY TO DO THIS, BUT THIS REPRESENTS POTENTIALLY A TRANSFORMATIVE LEAP FORWARD. I WOULD AGREE, THOUGH IT'S HIGH RISK, BUT IT'S EXTREMELY HIGH REWARD.

DR. JUELSGAARD: THANK YOU, JEFF. THANK YOU, DR. SAMBRANO. THAT'S HELPFUL. I APOLOGIZE FOR MONOPOLIZING THIS, BUT I'M DONE WITH MY QUESTIONS. THOSE ARE MY ISSUES.

MR. SHEEHY: ARE THERE OTHER QUESTIONS? DO WE HAVE ANY MEMBERS OF THE PUBLIC PRESENT? SO THE MOTION ON THE FLOOR IS TO ACCEPT THE RECOMMENDATIONS OF THE GRANTS WORKING GROUP AND TO FUND THIS PARTICULAR PROJECT. MARIA, COULD YOU CALL THE ROLL.

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: 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: DIANE WINOKUR.
MS. WINOKUR: YES.
MR. HARRISON: MOTION CARRIES.
MR. SHEEHY: SO THAT CONCLUDES THE BUSINESS OF THE APPLICATION REVIEW SUBCOMMITTEE. BACK TO YOU, CHAIRMAN THOMAS.
CHAIRMAN THOMAS: THANK YOU, MR. SHEEHY. WE WANT TO -- I KNOW YOU ASKED IF THERE WERE ANY MEMBERS OF THE PUBLIC PRESENT, BUT JUST FOR THE SAKE OF COVERING ALL BASES HERE, IS THERE ANY PUBLIC COMMENT IN GENERAL AT THIS TIME? HEARING NONE, I

WOULD LIKE TO REMIND EVERYBODY THAT OUR NEXT MEETING IS IN PERSON. IT WILL BE MARCH 16TH UP HERE WHERE --

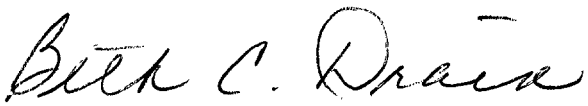
MS. CHEUNG: WESTIN SFO. YOU'LL SEE AN E-MAIL FROM ME SHORTLY.

CHAIRMAN THOMAS: WESTIN SFO. THANK YOU VERY MUCH, AMY. SO I BELIEVE THAT CONCLUDES TODAY'S MEETING. THANK EVERYBODY FOR ATTENDING, AND THE MEETING STANDS ADJOURNED.

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

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE AND THE APPLICATION REVIEW SUBCOMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS TELEPHONIC MEETING ON FEBRUARY 18, 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.



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