BEFORE THE

INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
AND 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: APRIL 29, 2019
12 P.M.

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

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I N D E X

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MONDAY, APRIL 29, 2019

12:00 P.M.

CHAIRMAN THOMAS: WELCOME, EVERYBODY, TO THE APRIL MEETING OF THE INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE AND APPLICATION REVIEW SUBCOMMITTEE FOR CIRM. LIKE TO CALL THE MEETING TO ORDER. PROCEED TO ROLL CALL. MARIA.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: PRESENT.

MS. BONNEVILLE: STEVE JUELSGAARD.

DR. JUELSGAARD: HERE.

MS. BONNEVILLE: SHERRY LANSING. DAVE MARTIN.

DR. MARTIN: HERE.

MS. BONNEVILLE: LAUREN MILLER.

MS. MILLER: HERE.

MS. BONNEVILLE: ADRIANA PADILLA.

DR. PADILLA: HERE.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: HERE.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: HERE.
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: DIANE WINOKUR.
MS. WINOKUR: HERE.
MS. BONNEVILLE: ARE THERE ANY OTHER BOARD MEMBERS ON THE LINE WHOSE NAME I DID NOT CALL?
DR. ZIEDONIS: YES. DOUG ZIEDONIS, Z-I-E-D-O-N-I-S.
DR. SANDMEYER: SUZANNE SANDMEYER.
MS. BONNEVILLE: IS THAT ALL? OKAY. I THINK WE ARE READY TO START. WE HAVE A QUORUM.
CHAIRMAN THOMAS: THANK YOU, MARIA. I'D LIKE TO GO IMMEDIATELY TO ITEM 3, CONSIDERATION OF APPLICATIONS SUBMITTED IN RESPONSE TO CLINICAL TRIAL STAGE PROJECTS CLIN1, 2, OR 3. TURN THE MEETING AT

THIS POINT OVER TO MR. SHEEHY.

MR. SHEEHY: THANK YOU, CHAIRMAN THOMAS. DR. SAMBRANO, ARE YOU TAKING US THROUGH THIS TODAY OR IS DR. PATEL?

DR. SAMBRANO: I AM.

MR. SHEEHY: THANKS, GIL. IF YOU'D LIKE TO GO AHEAD WITH THE PRESENTATION.

DR. SAMBRANO: OKAY. THANK YOU, MR. SHEEHY.

SO GOOD MORNING, EVERYONE, OR ALMOST AFTERNOON. TODAY WE ARE BRINGING FOR YOUR CONSIDERATION THREE APPLICATIONS FROM OUR LAST CLINICAL REVIEW. WE HAVE ONE APPLICATION THAT'S RESPONDING TO THE CLIN1, WHICH IS TO FUND LATE STAGE PRECLINICAL WORK, AND TWO APPLICATIONS FOR CLIN2, WHICH FUNDS CLINICAL TRIALS.

A VERY QUICK REMINDER OF THE SCORING SYSTEM THAT IS USED. ALL APPLICATIONS ARE SCORED ON A SYSTEM OF 1, 2, OR 3, WITH 1 BEING THOSE THAT RECEIVED EXCEPTIONAL MERIT AND WARRANT FUNDING. THOSE THAT GET A SCORE OF 2 USUALLY ARE PROMISING, BUT NEED IMPROVEMENT, AND THOSE GIVE THE APPLICANT THE OPPORTUNITY TO GO BACK TO THE GRANTS WORKING GROUP TO ADDRESS THOSE; AND A SCORE OF 3, THOSE THAT ARE SUFFICIENTLY FLAWED THAT DON'T COME BACK FOR SIX

MONTHS.

SO WE HAVE THREE APPLICATIONS. ONE OF THE APPLICATIONS FALLS UNDER OUR SICKLE CELL DISEASE CLINICAL PROGRAM. AND SO AS YOU MAY RECALL, AT THE ONSET OF THIS YEAR, WE SPLIT THE BUDGET ALLOCATION BETWEEN OUR SICKLE CELL PROGRAMS AND OTHER. AND SO I'M GOING TO GO FIRST OVER THE SICKLE CELL PROGRAM AND THAT APPLICATION, AND THEN I'LL SUBSEQUENTLY PRESENT THE BUDGET AND APPLICATIONS FOR THE NON-SICKLE CELL.

UNDER THE SICKLE CELL DISEASE PROGRAM, THIS IS THE FIRST ONE TO BE CONSIDERED, AND WE ALLOCATED $30 MILLION FOR THAT. THE AMOUNT THAT'S REQUESTED BY THE APPLICANT IS 4.5 MILLION. IF YOU WERE TO APPROVE THIS, WE WOULD COMMIT THIS AMOUNT AND LEAVE 25.5 MILLION IN THAT BUCKET. HOWEVER, BECAUSE THIS IS A PROGRAM IN COLLABORATION WITH THE NHLBI, OUR EXPECTATION IS THAT NHLBI WILL BE CO-FUNDING THIS PROJECT WITH US. RIGHT NOW THEY ARE IN THEIR FINAL FUNDING CONSIDERATION FOR THIS PROGRAM. SO WE DON'T HAVE A FINAL-FINAL WORD, BUT THEY HAVE LOOKED AT THIS APPLICATION FAVORABLY. SO WE EXPECT THAT IT WILL COME. SO IT WILL, UNDER THAT EXPECTATION, REDUCE THE AMOUNT OF COMMITMENT FROM CIRM POSSIBLY TO 50 PERCENT OF 4.5.

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SO THAT'S BUDGET OVERALL. IN TERMS OF TARGET NUMBERS FOR THE SICKLE CELL PROGRAM, WE ARE TARGETING FOR THIS YEAR FOUR CLINICAL TRIALS AND ONE CLIN1. THIS IS A CLIN1, SO WOULD MEET THE TARGET FOR THIS YEAR FOR CLIN1 PROGRAMS UNDER SICKLE CELL.

SO A SUMMARY OF THIS PROPOSAL. THIS IS CLIN1-1497. AND THE THERAPY IS AN AUTOLOGOUS CHRISPR-EDITED HEMATOPOIETIC STEM CELL THERAPY FOR PATIENTS WITH SICKLE CELL DISEASE. THE GOAL IS TO COMPLETE IND-ENABLING WORK AND TO FILE AN IND. AND THE TOTAL AMOUNT REQUESTED IS 4.5 MILLION.

A LITTLE BIT OF BACKGROUND ON THE DISEASE INDICATION AND THE VALUE PROPOSITION. SO AS MANY OF YOU KNOW, SICKLE CELL DISEASE AFFECTS ABOUT A HUNDRED THOUSAND AMERICANS. IT IS MOST COMMON IN SUB-SAHARAN AFRICAN ANCESTRY INDIVIDUALS, SO AFFECTING ABOUT ONE IN 365 BIRTHS, AND GLOBALLY ABOUT 300,000 ARE BORN WITH SICKLE CELL DISEASE EVERY YEAR.

THE VALUE PROPOSITION OF THIS THERAPY IS THAT THE ONLY AVAILABLE CURE CURRENTLY IS AN ALLOGENEIC HSC TRANSPLANTATION, WHICH CAN BE DIFFICULT FOR A VARIETY OF REASONS IN TERMS OF HAVING THE RIGHT DONOR. AND SO THE AVAILABILITY OF DONORS IS DIFFICULT TO GET, GRAFT VERSUS HOST

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DISEASE, GRAFT FAILURE. ALL OF THESE THINGS MAKE IT MUCH MORE DIFFICULT AND COMPLEX. THIS IS AN AUTOLOGOUS THERAPY WHICH WOULD TAKE THE PATIENT'S OWN HEMATOPOIETIC STEM CELLS AND WOULD OBVIATE MANY OF THESE LIMITATIONS. SO CERTAINLY WOULD BROADEN THE PATIENTS THAT THIS COULD REACH AS WELL.

SO WHY IS THIS A STEM CELL PROJECT? THIS THERAPY INCLUDES GENETICALLY MODIFIED HEMATOPOIETIC STEM CELLS. SO THAT'S WHY IT QUALIFIES FOR CIRM FUNDING.

THIS NEXT SLIDE SHOWS YOU WHERE THE PROJECT FITS INTO OUR OVERALL PORTFOLIO. CIRM IS FUNDING SEVERAL PROJECTS IN SICKLE CELL DISEASE. TWO OF THEM ARE CLINICAL TRIALS, BUT THEY HAVE DIFFERENT APPROACHES. ONE USES A LENTIVIRAL VECTOR TO TRANSFER AN ANTI-SICKLING GENE. ANOTHER ONE IS WORKING ON ADVANCING A PROTOCOL THAT ALLOWS FOR IMMUNE TOLERANCE THROUGH MIXED CHIMERISM THAT WOULD IMPROVE THE TRANSPLANT OF THE -- ALLOGENEIC TRANSPLANT FOR PATIENTS.

AND THEN WE HAVE ANOTHER APPROACH THAT'S ALSO IN A CLIN1 THAT USES CRISPR EDITING SIMILAR TO THIS CURRENT PROPOSAL, BUT THE BIG DIFFERENCE IS THAT THE CURRENT PROPOSAL USES A VIRUS-FREE CRISPR EDITING TECHNOLOGY THAT MAY HAVE SOME ADVANTAGES.

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IN TERMS OF PREVIOUS CIRM FUNDING, SO THIS APPLICANT HAS HAD A TRAN1, SO A TRANSLATION STAGE PROGRAM, THAT HAS BROUGHT THEM NOW TO THE STAGE WHERE THEY CAN DO IND-ENABLING WORK. THAT AWARD WAS ABOUT 4.5 MILLION. THEY WERE ON TRACK AND ACHIEVED MILESTONES PRETTY MUCH ALL THE WAY THROUGH IN THAT PREVIOUS AWARD.

SO THE GWG REVIEWED THIS APPLICATION, GAVE IT A SCORE OF 1 WITH 14 MEMBERS GIVING A SCORE OF 1 AND (INAUDIBLE) SCORE OF 2. AND SO THE CIRM TEAM RECOMMENDS THIS FOR THE FUNDING IN THE AMOUNT OF 4.5 MILLION. MR. SHEEHY.

MR. SHEEHY: THANK YOU, DR. SAMBRANO.

DO I HAVE A MOTION TO EITHER ACCEPT THE TEAM RECOMMENDATION OR TO NOT ACCEPT THE RECOMMENDATION AND EITHER TO FUND OR NOT FUND THIS APPLICATION?

MR. TORRES: MOTION TO ACCEPT AND FUND THE APPLICATION.

MR. SHEEHY: THANK YOU, SENATOR TORRES. DO I HAVE A SECOND?

DR. DULIEGE: I SECOND.

MR. SHEEHY: THANK YOU, DR. DULIEGE.

IS THERE ANY DISCUSSION BY BOARD MEMBERS ABOUT THIS APPLICATION?

DR. MARTIN: CAN YOU REVEAL TO US WHAT THE PROCESS IS FOR THE NONVIRAL TRANSDUCTION SYSTEM?

DR. SAMBRANO: THEY DO A DIRECT CRISPR-CAS9 ON THE CELLS. SO THEY JUST AVOID HAVING TO DO A SELECTION PROCESS THROUGH WHICH THEY WOULD DO IF THEY USE A VIRAL VECTOR. SO THEY'RE JUST BASICALLY DOING IT DIRECTLY ON THE CELL.

DR. MARTIN: A VECTOR OPERATION?

DR. SAMBRANO: YES.

DR. MARTIN: IT'S JUST NAKED DNA? THE REASON I'M ASKING IS BECAUSE THERE IS SOME TECHNOLOGY THAT IS FARTHER ALONG THAN JUST NAKED DNA. AND I JUST WONDER WHETHER THAT'S BEEN CONSIDERED BY THE APPLICANT.

DR. SAMBRANO: I DON'T WANT TO GO INTO TOO MUCH DETAIL ABOUT THEIR SYSTEM. IF THE APPLICANT WERE HERE, THAT WOULD BE UP TO THEM IF THEY WANT TO GO INTO THAT LEVEL OF DETAIL. IF YOU FEEL IT'S IMPORTANT, WE CAN DO THAT.

DR. MARTIN: IT'S MORE CURIOSITY AND BUILDING MORE CONFIDENCE. IT LOOKS GOOD. I'M NOT OBJECTING TO IT. I'M JUST CURIOUS AS TO WHETHER WE CAN REALLY EXPECT THIS TO BE ANOTHER BREAKTHROUGH.

MR. SHEEHY: ARE THERE ANY ADDITIONAL QUESTIONS OR COMMENTS FROM BOARD MEMBERS?

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DR. DULIEGE: NOPE. PRETTY STRAIGHTFORWARD APPLICATION.

MR. SHEEHY: DO WE HAVE ANY PUBLIC COMMENT AT ANY OF THE SITES?

MS. BONNEVILLE: WE DON'T HAVE ANY HERE.

MR. SHEEHY: GREAT. THANK YOU.

THEN LET'S CALL THE ROLL AND PROCEED TO A VOTE 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: DAVE MARTIN.

DR. MARTIN: 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.

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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: THANK YOU.
I THINK IT'S BACK TO YOU, DR. SAMBRANO, TO DISCUSS THE NEXT APPLICATION PLEASE.
DR. SAMBRANO: THANK YOU, MR. SHEEHY.
SO NOW LOOKING AT THE BUDGET FOR CLIN2 APPLICATIONS AND WHERE THEY SIT. SO WE HAD AN ANNUAL ALLOCATION OF 93 MILLION FOR NON-SICKLE CELL PROGRAMS. THERE'S BEEN 25.7 THAT HAS BEEN COMMITTED THUS FAR. IF YOU TODAY APPROVE THE TWO APPLICATIONS UNDER CONSIDERATION, WE WOULD ADD 11.3 MILLION, LEAVING US WITH 57 MILLION IN THAT POT.

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IN TERMS OF THE NUMBER OF AWARDS THAT WE ARE TARGETING, THIS WOULD ADD TWO CLINICAL TRIALS, MAKING IT A TOTAL OF FOUR OUT OF EIGHT THAT WE ARE TARGETING.

SO THE FIRST PROJECT UNDER CONSIDERATION IS CLIN2-11480, AND THIS IS AN AUTOLOGOUS CD18 GENE-MODIFIED HEMATOPOIETIC STEM CELL THERAPY FOR PATIENTS WITH LEUKOCYTE ADHESION DEFICIENCY 1. THE GOAL IS TO COMPLETE A PHASE 1/2 TRIAL, AND THEY ARE ASKING FOR 6.6 MILLION IN FUNDING AND PROVIDING 5.6 IN CO-FUNDING.

SOME BACKGROUND ON THIS CLINICAL INDICATION. SO THE LEUKOCYTE ADHESION DEFICIENCY 1 IS A RARE AUTOSOMAL RECESSIVE DISORDER THAT OCCURS ABOUT ONE IN A MILLION PEOPLE NATIONWIDE. AND IT IS AN IMMUNE DEFICIENCY, AND MOST CHILDREN WITH THE SEVERE FORM WILL DIE FROM INFECTIONS BEFORE THE AGE OF TWO.

SO THE VALUE PROPOSITION THAT THIS OFFERS, THE ONLY CURRENT CURE IS AN ALLOGENEIC HSC TRANSPLANT, SO SIMILAR TO THE SICKLE CELL. THERE ARE THOSE LIMITATIONS THAT COME WITH AN ALLOGENEIC TRANSPLANT, INCLUDING TRYING TO FIND APPROPRIATE DONORS AND SO FORTH. THIS WOULD BE A GENE CORRECTION GENE THERAPY THAT WOULD RESTORE IMMUNE

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FUNCTION AND CERTAINLY WOULD BE SOMETHING THAT IS NOT CURRENTLY AVAILABLE TODAY.

WHY IS THIS A STEM CELL PROJECT? THERAPY INCLUDES GENETICALLY MODIFIED HEMATOPOIETIC STEM CELLS.

FOR THIS PARTICULAR PROJECT, WE REALLY DON'T HAVE ANY OTHER PROJECTS IN THIS INDICATION. WE HAVE SOME THAT ARE RELATED IN TERMS OF THE TYPE OF APPROACH, BUT NOTHING IN THIS CLINICAL ARENA.

IN TERMS OF PREVIOUS FUNDING, THE APPLICANT HAS NOT HAD PREVIOUS CIRM FUNDING. SO THAT TAKES US TO THE GRANTS WORKING GROUP REVIEW SUMMARY. THE GRANTS WORKING GROUP UNANIMOUSLY RECOMMENDED THIS APPLICATION WITH A SCORE OF 1. AND CIRM TEAM RECOMMENDS FUNDING IN THE AWARD AMOUNT OF 6.6 MILLION.

MR. SHEEHY: THANK YOU, DR. SAMBRANO.

SO DO I HAVE A MOTION TO EITHER ACCEPT THE TEAM'S RECOMMENDATION AND FUND THIS PROJECT OR TO NOT ACCEPT THE RECOMMENDATION AND NOT TO FUND IT?

DR. PRIETO: MOVE TO FUND.

MR. SHEEHY: THANK YOU, DR. PRIETO.

DO I HAVE A SECOND?

MR. ROWLETT: SECOND.

MR. SHEEHY: THANK YOU, AL.

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OKAY. DO WE HAVE ANY BOARD COMMENTS OR QUESTIONS?

MR. TORRES: YES. JUST ONE QUESTION. WHY WAS IT TAKEN OUT OF ORDER? WAS THERE A REASON FOR THAT? THE NEXT ONE, AT LEAST ON THE AGENDA, SHOWS 11380. YOU JUST DID IT ON YOUR OWN?

DR. SAMBRANO: I DID IT ALL ON MY OWN.

MR. TORRES: I WAS WONDERING IF THERE WAS A SUBSTANTIVE REASON.

DR. SAMBRANO: NO.

MR. SHEEHY: OTHER QUESTIONS OR COMMENTS?

DR. MARTIN: THERE'S AN APPARENT ISSUE HERE THAT IS OBVIOUSLY TROUBLING TO RAISE OR TO IGNORE, AND THAT IS THIS IS A VERY RARE DISEASE. AND WITH WHAT I ANTICIPATE, ANYWAY, BEING SOMEWHAT LIMITED FUNDING FOR THE REST OF THIS PARTICULAR ENTIRE PROGRAM. I WONDER ABOUT JUST HOW SHOULD WE DEAL WITH THIS? MAYBE IT WILL WORK; MAYBE IT WON'T, AND WE HAVEN'T DONE THIS ONE BEFORE.

THE OTHER THING IS, AS A FORMER MEDICAL GENETICIST, WHAT ONE ALWAYS THINKS ABOUT IS THE DISEASE BURDEN. AND THIS MAY SOUND INHUMANE, BUT THIS IS A RELATIVELY LOW BURDEN DISEASE. LOW BURDEN IN THE CONTEXT OF THIS IS NOT A LIFELONG BURDEN FOR 50 YEARS OR 30 YEARS OR SOMETHING OF THAT SORT.

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IT'S RELATIVELY SHORT BECAUSE THESE CHILDREN DO DIE IF THEY DON'T HAVE SOME TYPE OF A MATCH FOR HSC.

I JUST -- IT'S TROUBLING, AS I SAID, TO BRING IT UP OR TO IGNORE IT. I JUST WONDER WHAT THE THOUGHTS ARE OF OTHER BOARD MEMBERS ON THIS.

MR. SHEEHY: PERHAPS DR. SAMBRANO COULD ADD SOME CONTEXT ABOUT THE APPLICANT. IT IS AN INDUSTRY APPLICANT WITH A COMMERCIALIZATION PLAN. I DO THINK THAT PUTS IT IN A LITTLE BIT DIFFERENT CONTEXT THAN AN ACADEMIC RESEARCH EXERCISE THAT WOULDN'T NECESSARILY LEAD TO OTHER PROJECTS, INDICATIONS, OR TO A SUSTAINABLE BUSINESS MODEL THAT WOULD CONTINUE TO PRODUCE THESE CURES FOR THESE INDIVIDUALS ON INTO THE FUTURE.

DR. SAMBRANO: I'M NOT SURE WHAT I CAN ADD TO WHAT MR. SHEEHY JUST SAID OTHER THAN, YES, THEY ARE DEFINITELY A FOR-PROFIT COMPANY, HAVE A PLAN FOR DEVELOPMENT. AND SO TO THE EXTENT THAT THAT IS A CONSIDERATION, THAT IS ABSOLUTELY THE CASE.

MR. SHEEHY: DO OTHER MEMBERS HAVE ANY THOUGHTS ON THIS? OKAY.

DO WE HAVE ANY PUBLIC COMMENT FROM ANY OF THE SITES?

DR. DULIEGE: ONE QUESTION FROM ANNE-MARIE. IT SAYS IT'S A PHASE 2 TRIAL

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COMPLETION. MAYBE CAN WE GET A LITTLE BIT OF UPDATE ON THE PHASE 2 TRIAL INITIATION? IS IT GOING ON TARGET? AND WHAT'S THE COMPLETION? I UNDERSTAND THAT THE FUNDING IS ABOUT $6.6 MILLION. IF WE CAN GET A LITTLE BIT MORE EXPLANATION ABOUT THE COMPLETION.

DR. SAMBRANO: SO THE APPLICATION WOULD ACTUALLY FUND WHAT THEY'RE CALLING A PHASE 1/2 TRIAL. SO THEY HAVE NOT YET STARTED WITH ANY PATIENTS. THEY WOULD HAVE TWO COHORTS. THEY WOULD START WITH -- IN TOTAL IT'S GOING TO BE A VERY SMALL NUMBER OF PATIENTS BECAUSE OF THE RARITY OF THE DISEASE. BUT THEY WOULD START WITH A COUPLE OF PATIENTS IN ORDER TO ENSURE SAFETY AND THEN WOULD GO ON TO THE PHASE 2 COHORT FROM THERE IN ORDER TO ASSESS EFFICACY. AND THE TOTAL NUMBER IS UNDER TEN. SO OUR FUNDING WOULD INITIATE THE TRIAL.

DR. SCHWARTZ: GOOD MORNING, GOOD AFTERNOON. THIS IS DR. JONATHAN SCHWARTZ. I'M THE CHIEF MEDICAL OFFICER OF ROCKET PHARMA, WHICH IS THE SPONSOR OF THE INITIATIVE.

I JUST WANTED TO EMPHASIZE THAT, ALTHOUGH LEUKOCYTE ADHESION DEFICIENCY 1 IS A VERY RARE DISORDER, IT IS NONETHELESS ONE OF THE MOST SEVERE IMMUNODEFICIENCIES THAT IS KNOWN, AS THE DISCUSSION

HAS INDICATED. I THINK IT'S IMPORTANT TO EMPHASIZE THAT THIS FALLS WITHIN A SPECTRUM OF NEUTROPHIL-MEDIATED IMMUNODEFICIENCIES.

THE PRINCIPAL INVESTIGATOR AND GLOBAL STUDY LEAD FOR THIS INITIATIVE, DR. DONALD KOHN AT UCLA, IS ALSO THE PRINCIPAL INVESTIGATOR ON ANOTHER IMMUNODEFICIENCY DISORDER THAT AFFECTS LEUKOCYTES, SPECIFICALLY NEUTROPHILS. IT'S A CHRONIC GRANULOMATOUS DISEASE STUDY WHICH IS UNDER WAY AND IS APPEARING TO BE QUITE SUCCESSFUL AS PRELIMINARY DATA HAVE BEEN PRESENTED OVER THE PAST TWO YEARS.

THIS STUDY, IN FACT, UTILIZES A VECTOR THAT MAKES USE OF AN IDENTICAL VIRAL PROMOTER. AND, THEREFORE, WE HAVE A REASONABLE DEGREE OF CONFIDENCE THAT THIS HAS A GOOD PROBABILITY OF SUCCESS.

I WOULD ALSO EMPHASIZE THAT ROCKET PHARMA AND OUR ACADEMIC PARTNERS HAVE FDA BUY-IN THAT, BECAUSE OF THE DISORDER'S RARITY AND EXTREME SEVERITY, THAT THIS MODESTLY SIZED STUDY THAT IS APPROXIMATELY TEN PATIENTS WOULD BE SUFFICIENT FOR MARKETING AUTHORIZATION IF THE RESULTS ARE FAVORABLE.

SO I THINK, ALTHOUGH IT'S A VERY RARE DISEASE, WE'RE MAKING A VERY EFFICIENT USE OF RESOURCES. AND I THINK, JUST AS AN ADDITIONAL

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POINT, KNOWLEDGE GAINED FROM THIS ENDEAVOR IS LIKELY TO IMPACT OUR ABILITY AS A COLLECTIVE GROUP, ACADEMICS AND INDUSTRY SPONSORS, TO DEVELOP ADDITIONAL GENE THERAPIES FOR OTHER DISORDERS AFFECTING WHITE BLOOD CELLS. SO IF WE ARE SUCCESSFUL HERE, THIS IS LIKELY TO BEGET ADDITIONAL INITIATIVES IN OTHER RARE AND PERHAPS NOT-SO-RARE DISORDERS.

ONE ADDITIONAL JUST COMMENT IS THAT THE STUDY IS CURRENTLY OPEN AT UNIVERSITY OF CALIFORNIA LOS ANGELES, AND THE FIRST PATIENT IS SCHEDULED TO BEGIN TREATMENT OVER THE COMING WEEKS.

MR. SHEEHY: THANK YOU. DO WE HAVE ANY QUESTIONS OR COMMENTS?

DO WE HAVE ANY MORE PUBLIC COMMENT?

COULD WE CALL THE ROLL 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: DAVE MARTIN.

DR. MARTIN: I'LL ABSTAIN IF I MAY.

MS. BONNEVILLE: LAUREN MILLER.

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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: ABSTAIN.
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: ABSTAIN.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
MS. BONNEVILLE: MOTION CARRIES.
MR. SHEEHY: THANK YOU.
DR. SAMBRANO, THE NEXT APPLICATION PLEASE.
DR. SAMBRANO: THANK YOU, MR. SHEEHY.

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THE NEXT APPLICATION IS CLIN2-11380. AND THIS THERAPY IS AN AUTOLOGOUS GENE-MODIFIED HEMATOPOIETIC STEM AND T-CELL COMBINATION EXPRESSING A T-CELL RECEPTOR THAT RECOGNIZES NY-ESO-1. SO THE INDICATION, THESE WOULD BE PATIENTS WITH SARCOMAS THAT ARE POSITIVE FOR THAT MARKER. AND THEIR GOAL IS TO COMPLETE A PHASE 1 CLINICAL TRIAL AND ARE REQUESTING $4.7 MILLION IN FUNDING.

SO A LITTLE BIT ABOUT THE BACKGROUND. SO SYNOVIAL SARCOMA IS RARE, AFFECTS YOUNG ADULTS, AND THERE ARE ABOUT 8 TO 900 WHO ARE DIAGNOSED WITH THE DISEASE IN THE U.S. EACH YEAR. AND THOSE THAT HAVE LOCAL ADVANCED OR METASTATIC TUMORS HAVE POOR PROGNOSIS AND LOW SURVIVAL.

THE VALUE PROPOSITION FOR THIS IS THAT THERE ARE ALSO CERTAINLY NO TREATMENT OPTIONS AVAILABLE TO THESE PATIENTS, ESPECIALLY THOSE THAT HAVE EXHAUSTED SURGERY AND CHEMOTHERAPY. THE PROPOSAL DUAL CELL THERAPY IMPROVES SURVIVAL, AND IT HAS BOTH AN IMMEDIATE IMPACT ON THE TUMOR THROUGH THE ADMINISTRATION OF MATURE T-CELLS THAT ARE TARGETING THE TUMOR, AS WELL AS A MORE SUSTAINED AND MAYBE MORE PERMANENT ANTI-TUMOR THROUGH ENGRAPHMENT OF HEMATOPOIETIC STEM CELLS THAT WOULD THEN GENERATE T-CELLS THAT WOULD ACT ON THE TUMOR.

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WHY IS THIS A STEM CELL PROJECT? THE THERAPY INCLUDES GENETICALLY MODIFIED HEMATOPOIETIC STEM CELLS AS BEFORE.

WHERE THIS FITS INTO OUR PORTFOLIO, THERE IS ONE OTHER PROJECT THAT IS BY THE SAME OVERALL TEAM. IT WAS A DISEASE TEAM AWARD THAT WAS GIVEN WITH THE SAME PRODUCT AND IS CURRENTLY FOR MULTIPLE MYELOMA WHERE THIS ONE IS FOCUSED ON SARCOMA.

SO THEN A LITTLE BIT ABOUT THE PREVIOUS FUNDING. SO AS I INDICATED, THAT OTHER PROJECT IN OUR PORTFOLIO IS VERY SIMILAR. SO THAT ONE IS AN ONGOING DISEASE TEAM PROJECT. ORIGINALLY RECEIVED ABOUT 20 MILLION AND HAVE USED UP, THUS FAR, ABOUT 4.2.

THE PROJECT STARTED OUT ACTUALLY AS A PROPOSAL THAT INCLUDED SOLID TUMOR SARCOMA ORIGINALLY. IT WENT THROUGH SOME DELAYS IN TERMS OF RECRUITMENT AND EVENTUALLY SWITCHED OVER TO MULTIPLE MYELOMA FOR SEVERAL REASONS AS A POTENTIALLY BETTER PATIENT POPULATION UNDER THAT AWARD. THERE ARE STILL SOME DELAYS WITH IT THAT EXIST. SO CIRM IS WORKING WITH THEM THROUGH THAT. AND SO THAT'S THE PREVIOUS CIRM FUNDING.

FROM THE REVIEWS, SO THE GWG REVIEWED THIS APPLICATION. THEY GAVE IT A SCORE OF 1 WITH 14

MEMBERS SCORING A 1 AND 1 MEMBER GIVING IT A SCORE OF 2. CIRM TEAM OVERALL RECOMMENDATION IS TO FUND THE AWARD OF 4.7 MILLION.

MR. SHEEHY: THANK YOU, DR. SAMBRANO.

DO WE HAVE A MOTION TO EITHER ACCEPT THE TEAM RECOMMENDATION AND FUND THIS PROJECT OR TO NOT ACCEPT THE TEAM RECOMMENDATION AND NOT FUND THIS PROJECT?

MR. TORRES: AS A REVIEWER FOR THIS PROJECT, I WHOLEHEARTEDLY ENDORSE AND MOVE IT TO BE APPROVED.

MR. SHEEHY: THANK YOU, SENATOR TORRES.

DO WE HAVE A SECOND?

CHAIRMAN THOMAS: SECOND.

MR. SHEEHY: SECONDED BY CHAIRMAN THOMAS. DO WE HAVE BOARD DISCUSSION? QUESTIONS, COMMENTS?

DR. JUELSGAARD: I HAVE A COUPLE OF QUESTIONS FOR DR. SAMBRANO.

I WANT TO GO BACK TO THE LAST SLIDE, THE ONE THAT TALKS ABOUT THEIR EFFORTS TO DATE REGARDING THE PREVIOUS INDICATION THAT THEY'RE PURSUING. YOU MADE A COMMENT THAT THEY ORIGINALLY STARTED WITH SARCOMA AND FOUND THAT DIFFICULT AND SWITCHED TO MULTIPLE MYELOMA. WHAT MAKES ONE THINK THAT THINGS HAVE CHANGED REGARDING SARCOMA? WHAT WAS THE

DIFFICULTY, AND WHY IS IT NOT GOING TO BE A DIFFICULTY THIS TIME?

DR. SAMBRANO: SO THAT'S A VERY GOOD QUESTION. SO THIS IS SOMETHING THAT DID COME UP DURING REVIEW. AND SO THE RESPONSE THAT THEY PROVIDED WAS THAT, AT LEAST TODAY COMPARED TO IN THE PAST, THAT THEY HAVE DONE ADDITIONAL OUTREACH. THEY HAD A PROGRAM -- THERE WAS INTEREST EXPRESSED BY PATIENTS. AND SO THEY HAVE LINED UP A HANDFUL OF PATIENTS THAT THEY FEEL CAN PARTICIPATE. AND THEY'VE DOSED THEIR FIRST PATIENT. SO THEY FEEL THAT THEY CAN OVERCOME THAT. AT LEAST FOR THE GRANTS WORKING GROUP, IT WAS SUFFICIENT FOR THEM TO BE OKAY WITH IT.

DR. JUELSGAARD: THEN THE SECOND QUESTION. ON THE SLIDE IN THE RIGHT-HAND COLUMN UNDER MILESTONES, IT'S CALLED OM3. I'M NOT EXACTLY SURE WHAT THE O STANDS FOR, BUT I IMAGINE THAT WAS A MILESTONE 3.

IT TALKS ABOUT DELAY WITH SERIOUS CONCERNS. CAN YOU PLEASE EXPLAIN WHAT SERIOUS CONCERNS RELATES TO? SERIOUS CONCERNS TO ME ARE SERIOUS, RIGHT. SO WHAT'S GOING ON?

DR. SAMBRANO: RIGHT. SO I CAN TELL YOU IN GENERAL WHAT THE DELAYS WERE. SO THERE WERE

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DELAYS RELATED TO ENROLLMENT, BUT ALSO DELAYS THAT WERE RELATED TO ADVICE FROM A CDAP, THE CLINICAL DEVELOPMENT ADVISORY PANEL, THAT WE HAD AT THE TIME FOR THE DISEASE TEAM PROGRAMS WHERE THE APPLICANT SUGGESTED THE CHANGE IN INDICATION TO MULTIPLE MYELOMA. THAT WAS ACCEPTED. AND SO PART OF THE DELAY WAS ALSO IN KIND OF REDIRECTING THE PROJECT TO THAT NEW INDICATION. SO SOME OF THE DELAYS CAME THERE.

AND TREATING THE FIRST SUBJECT DID NOT HAPPEN FOR A WHILE, WHICH MAY HAVE BEEN A RESULT OF THOSE THINGS. SO WE CAN CERTAINLY HAVE THE SCIENCE OFFICER INVOLVED IN MANAGING THE PROJECT IF YOU WANT MORE DETAIL THAN THAT TO GIVE YOU A LITTLE MORE OF EXACTLY WHY THE SERIOUS CONCERN.

DR. JUELSGAARD: LET ME JUST MAKE TWO OBSERVATIONS THAT I GUESS CONCERN ME. THE FIRST IS JUST THE FACT THAT WHAT WE'VE GOT IS EXACTLY THE SAME POTENTIAL THERAPEUTIC AGENT BEING TESTED NOW CONCURRENTLY AT TWO DIFFERENT INDICATIONS. AND THE QUESTION IS IS THAT A WISE USE OF MONEY? BECAUSE THE ALTERNATIVE WOULD BE GET PROOF OF CONCEPT DATA FROM THE FIRST THERAPEUTIC AREA THAT IS MULTIPLE MYELOMA AND SEE IF IT SHOWS A POSITIVE EFFECT AND THEN WITH THAT, AND THAT WOULD BE AT THE END OF

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PHASE 2, WITH THAT, THEY'D BE ABLE TO ADVANCE FORWARD INTO OTHER INDICATIONS, INCLUDING SARCOMA. MORE OF A STEPWISE APPROACH AS OPPOSED TO A CONCURRENT APPROACH.

THE SECOND, AND THIS IS JUST A GENERAL OBSERVATION OF THINGS THAT MAY HAPPEN AS WE'RE GOING ALONG HERE, IT'S NOT, I THINK, LOST ON THE OUTSIDE WORLD THAT WE ARE BECOMING INCREASINGLY SHORT ON MONEY, AND AS OF YET THERE'S NO PROMISE THAT THERE WILL BE ADDITIONAL FUNDS AVAILABLE AFTER WE EXPEND WHAT WE HAVE.

ONE OF THE BEHAVIORS THAT THAT MIGHT DRIVE IS FOR PEOPLE TO RUSH IN WITH PROJECTS HOPING TO GET APPROVAL AND RECEIVE FUNDING BEFORE WE DO RUN OUT OF FUNDS AND PEOPLE SORT OF GETTING THE CART BEFORE THE HORSE; THAT IS, COMING IN WITH IDEAS FOR FUNDING THAT REALLY WOULD BE BETTER OFF ON BEING HELD BACK FOR A PERIOD OF TIME UNTIL MORE DATA IS DEVELOPED OR UNTIL THEY SHOW MORE ABILITY TO KIND OF MOVE FORWARD WITH THEIR CLINICAL EXPERIENCE, WHICH I FEAR IS SOMEWHAT THE CASE HERE, NOT KNOWING A LOT MORE ABOUT WHAT'S HAPPENING WITH THEIR CLINICAL DEVELOPMENT PLAN. RIGHT NOW IT'S NOT CONFIDENCE INSPIRING WHAT, I'M HEARING ANYWAY, ABOUT HOW WELL THEY'RE ABLE TO RUN A CLINICAL DEVELOPMENT PROGRAM.

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THOSE ARE JUST OBSERVATIONS. I DON'T HAVE ANY OTHER QUESTIONS.

DR. MARTIN: I HAVE A QUESTION JUST TO MAKE CERTAIN I UNDERSTAND THIS. THAT IS THAT THE TECHNOLOGY IN THE PREVIOUS NOW MM INDICATION AND THIS ONE IS ESSENTIALLY IDENTICAL; AND, THAT IS, YOU HAVE TO CHOOSE A DIFFERENT SOURCE OF THE STEM CELLS. SO YOU HAVE SOME TYPE OF HAPLOIDENTICAL DONOR. BUT THE TRANSDUCTION AND THE CONSTRUCT OF THE -- SO ONE VECTOR IS ESSENTIALLY THE SAME. IS THAT UNDERSTANDING VALID?

DR. SAMBRANO: BOTH ARE THE SAME. IT'S THE SAME THERAPEUTIC USING THE SAME T-CELL RECEPTOR TARGETING THE NY-ESO-1. AND THEY'RE USING IT IN EITHER CASE THE SAME WAY, EITHER TO TARGET MULTIPLE MYELOMA OR SOLID TUMORS. THE ADMINISTRATION WOULD BE THE ONLY THING THAT WOULD BE DIFFERENT, BUT OTHERWISE IDENTICAL.

DR. TALIB: THIS IS SOHEL TALIB, THE PROGRAM OFFICER. THIS IS AN AUTOLOGOUS APPROACH WHICH PATIENT'S OWN BLOOD-FORMING STEM CELLS ARE GENE MODIFIED, AND THEY BOTH TARGET ALL THE TUMOR WHICH ARE NY-ESO-1 POSITIVE, AS IN THE CASE OF CANCER AND IN THE CASE OF MULTIPLE MYELOMA, LIQUID CANCER, SO THEY'RE TARGETING NY-ESO-POSITIVE TUMOR.

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DR. MARTIN: IF THAT'S THE CASE, WHY NOT SIMPLY BROADEN THE ENTRY CRITERIA TO INCLUDE MM'S OR THE OTHER INDICATION, THE SARCOMA, IN THE SAME TRIAL? BECAUSE THE ONLY DIFFERENCE IS WHAT THE MALIGNANT DISEASE IS THAT THE DONOR, AUTOLOGOUS DONOR, PATIENT EXHIBITS. SO, THEREFORE, THE FUNDING WOULD BE THE SAME EXCEPT YOU JUST HAVE TO FILE AN ADDENDUM TO THE IND, I WOULD EXPECT.

DR. TALIB: THESE ARE TWO SEPARATE IND'S. SO THE INVESTIGATOR INDEED HAS TWO IND'S, ONE FOR MULTIPLE MYELOMA AND THE SECOND ONE, THE ONE WHICH IS BEING PROPOSED HERE FOR SARCOMA, THAT IS SEPARATE IND. SO THESE ARE TWO SEPARATE IND'S AND INDICATION ARE NY-ESO-POSITIVE TUMORS.

DR. MARTIN: HAVE YOU EXPLORED COMBINING THAT INTO A SINGLE IND BY AMENDING ONE OR THE OTHER?

DR. TALIB: I'M AFRAID I CANNOT ANSWER THE QUESTION, BUT THE PI FOR THIS CLINICAL TRIAL IS HERE IN THIS MEETING. PERHAPS IF YOU NEED MORE INFORMATION FROM THE INVESTIGATOR, HE'S HERE.

DR. NOWICKI: I'M DR. NOWICKI. I'M THE PRINCIPAL INVESTIGATOR FOR CIRM GRANT CLIN2-11380. IN RESPONSE TO THE QUESTION ABOUT COMBINING THE TWO IND'S, ACTUALLY THE FDA WILL NOT ALLOW US BECAUSE IT'S DIFFERENT DIVISIONS.

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MR. SHEEHY: DOES THAT ANSWER YOUR QUESTION, DR. MARTIN?

DR. MARTIN: YES, IT DOES, UNFORTUNATELY. I DON'T UNDERSTAND. I UNDERSTAND THE ISSUE OF DIFFERENT DIVISIONS. I'VE HAD EXPERIENCE TRYING TO DO THIS, AND IT'S A NEGOTIATION WITH THE AGENCY. IT'S SIMILAR, BUT OBVIOUSLY NOT IDENTICAL.

MR. SHEEHY: SINCE WE HAVE DR. NOWICKI, DO WE HAVE OTHER QUESTIONS FOR THE APPLICANT? MR. JUELSGAARD, IF YOU MIGHT WANT TO ASK SOME QUESTIONS OR YOU HAD SOME CONCERNS OR ANYBODY ELSE ON THE BOARD.

DR. JUELSGAARD: GIVEN THAT WE HAVE A REPRESENTATIVE FROM THE INSTITUTION THAT'S CONDUCTING THE TRIAL, SO GO BACK TO MY QUESTION ONE. WHY ARE YOU -- WHAT WAS THE DECISION PROCESS IN DECIDING TO CONCURRENTLY PURSUE SARCOMA AND MULTIPLE MYELOMA? WHY NOT JUST WAIT TO SEE WHAT YOUR PHASE 2 RESULTS ARE ON MULTIPLE MYELOMA, SEE IF YOU HAVE PROOF OF CONCEPT, AND THEN MAKE A DECISION ABOUT WHETHER TO PROCEED WITH SARCOMA OR NOT? WHY PROCEED WITH BOTH AT THIS POINT?

DR. NOWICKI: SO INITIALLY WE DID HAVE THE INDICATION FOR SARCOMA AND OTHER SOLID TUMORS. THAT WAS THE INITIAL APPROACH. WHAT HAD HAPPENED WAS WE

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WERE THEN MADE TO CHANGE THE INDICATION BY CIRM. WE WERE MADE TO CHANGE THE INDICATION FROM SOLID TUMOR SARCOMA TO MULTIPLE MYELOMA. AND, HOWEVER, AT THE TIME THAT THAT WAS HAPPENING, WE ALREADY RECRUITED THE FIRST PATIENT FOR SARCOMA AND WE WERE ABLE TO ADMINISTER THE TREATMENT SUCCESSFULLY. THERE WERE NO TOXICITIES. IT WAS ADMINISTERED VERY SAFELY, AND IT WAS A VERY SMOOTH PROCEDURE.

AND THE THING IS THAT BECAUSE WE HAD PUT FORTH SIGNIFICANT AMOUNT OF OUTREACH INTO THE SARCOMA POPULATION AND ALSO INTO OUR NETWORK OF CLINICIANS, UCLA BENG THE THIRD LARGEST SARCOMA CENTER IN THE COUNTRY AND THE LARGEST CENTER ON THE WEST COAST, WE WERE ABLE TO ACTUALLY BEGIN TO GET PATIENT INTEREST THAT WAS EXPRESSED TO US AND REFERRED TO US. AND FOR A WHILE, WE WERE CONTINUING TO SCREEN SUCH PATIENTS BECAUSE WE WERE UNCLEAR SORT OF WHERE THE DECISION WOULD FALL OUT FROM THAT. AND WE ACTUALLY WOUND UP HAVING TO TURN A NUMBER OF SARCOMA PATIENTS AWAY. ONCE THE INDICATION HAD BEEN CHANGED TO MYELOMA, WE NO LONGER HAD THE FUNDING FOR SARCOMA.

AND WE HAVE ACTUALLY EVEN GOT FURTHER CONTINUED. THOSE OUTREACH PROGRAMS HAVE RECENTLY BEEN MADE A REFERRAL CENTER FOR NY-ESO-1 POSITIVE

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SARCOMAS BY THE NATIONAL CANCER INSTITUTE SURGERY BRANCH. WE'D BEEN CONDUCTING THESE TRIALS AND NOW NO LONGER HAVE THE BANDWIDTH TO TREAT MANY PATIENTS. SO THEY WANT TO REFER ALL OF THEIR WEST COAST PATIENTS TO US NOW.

AND SO GIVEN THAT WE HAVE A SIGNIFICANT NUMBER OF PATIENTS THAT ARE COMING THROUGH THAT HAVE SUCH INTEREST IN THESE THERAPIES, WE'RE VERY KEEN TO CONTINUE THIS PROTOCOL AND TO SECURE FUNDING TO DO SO. AND WE'VE BEEN VERY FORTUNATE TO HAVE BEEN FUNDED BY CIRM IN THE PAST TO DO SO, AND THE PATIENT THAT WAS TREATED BEFORE CERTAINLY APPRECIATES THAT AND WE KNOW OUR FUTURE PATIENTS WOULD APPRECIATE IT AS WELL.

MR. SHEEHY: DOES THAT ANSWER YOUR QUESTIONS?

DR. JUELSGAARD: WITH ONE ADDITION. ARE YOU NOW TREATING -- THESE SARCOMA PATIENTS THAT YOU WOULD BE TREATING, ARE THOSE WHO HAVE HAD BOTH SURGERY AND CHEMOTHERAPY WITHOUT SUCCESS? BASICALLY THEIR CANCER REMAINS OR IS ADVANCING IN THE FACE OF BOTH SURGERY AND CHEMOTHERAPY? IS THAT THE COHORT YOU WOULD BE RECRUITING?

DR. NOWICKI: CORRECT.

DR. JUELSGAARD: WHAT PERCENTAGE OF THE

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SARCOMA POPULATION YOU WOULD BE SEEING WOULD NORMALLY FIT THAT CATEGORY OF FAILING BOTH THERAPIES?

DR. NOWICKI: JUST TO CLARIFY. BASICALLY WE CONSIDER METASTATIC DISEASE AS WELL AS CONSIDERING THAT WELL OVER HALF OF THESE PATIENTS ULTIMATELY GO ON TO DEVELOP METASTASIS. IT'S UNFORTUNATELY A VERY COMMON OCCURRENCE WITH THE SARCOMA POPULATION. AND THE ONES THAT HAVE MORE LOCALLY PROGRESSIVE DISEASE, LIKE A STAGE 3C, MIGHT HAVE FAILED SURGERY, HAVE FAILED CHEMOTHERAPY, OR OTHERWISE HAVE INOPERABLE DISEASE BECAUSE OF THE LOCATION. ONE OF THE WORST THINGS AS I TREAT SARCOMA, AND ONE OF THE WORST PARTS OF MY JOB IS BEING ABLE TO TELL THESE PATIENTS THAT THERE'S NOTHING MORE I CAN DO, THERE'S NOTHING MORE THAT I CAN TRY. AND THIS IMMUNOTHERAPY APPROACH WITH A STEM-CELL BASED APPROACH IS REALLY THE ONE OF A KIND THAT HAS THE ABILITY TO REALLY OFFER SOME HOPE TO THESE PATIENTS. SO ABSOLUTELY, UNFORTUNATELY, A VERY COMMON OCCURRENCE, I CAN TELL YOU.

DR. JUELSGAARD: ONE MORE QUICK QUESTION. SO THEN YOU HAVE THE CONFIDENCE THAT YOU HAVE THE PATIENT POPULATION OR YOU CAN RECRUIT THE PATIENT POPULATION NECESSARY TO PROCEED WITH THIS TRIAL IN

SARCOMA WITHOUT UNDUE DELAY?

DR. NOWICKI: I BELIEVE SO.

DR. JUELSGAARD: YOU FEEL CONFIDENT IN THAT?

DR. NOWICKI: I DO. AS I SAID, WE'VE HAD PATIENTS ACTIVELY AWAITING POTENTIAL ENROLLMENT IN THIS TRIAL THAT HAVE STILL EXPRESSED INTEREST FROM BEFORE WE HAD THE FUNDING SHUNTED TO MYELOMA. WE ALSO HAVE THE SUPPORT OF THE UCLA/UCI ALPHA STEM CELL CLINIC, WHICH HAS THE ABILITY TO ACCESS THE RECORDS OF 12 MILLION PATIENTS RESPECTIVE PATIENT IDENTIFICATION FURTHERMORE. AND AS I SAID BEFORE, UCLA IS THE THIRD LARGEST SARCOMA CENTER AND THE LARGEST ON THE WEST COAST. SO I DEFINITELY AM CONFIDENT IN OUR VOLUME.

DR. JUELSGAARD: THANK YOU VERY MUCH.

DR. NOWICKI: THANK YOU.

MR. SHEEHY: DO WE HAVE OTHER QUESTIONS FOR THE APPLICANT?

CHAIRMAN THOMAS: I'VE GOT ONE QUESTION. IN THE DOCUMENTATION IT REFERS TO THE FACT THAT THIS COULD BE USED FOR OTHER TYPES OF SOLID TUMORS WITH HIGH NY-ESO-1 EXPRESSION BESIDES SARCOMA. COULD YOU ELABORATE ON THAT FOR THE BENEFIT OF THE BOARD PLEASE?

DR. NOWICKI: ABSOLUTELY. THANK YOU. I'M GLAD YOU ASKED THAT QUESTION. WE TALK ABOUT SARCOMAS BECAUSE THESE ARE THE MOST FREQUENT TUMOR TYPES TO EXPRESS NY-ESO-1 SYNOVIAL SARCOMA AT A RATE OF GREATER THAN 80 PERCENT; BUT A MINORITY OF MELANOMAS, WHICH WE KNOW ARE CERTAINLY COMMON, EXPRESS NY-ESO ON THE ORDER OF ABOUT 30 PERCENT. AS I MENTIONED BEFORE, I'M A PEDIATRIC ONCOLOGIST. AND NEUROBLASTOMAS, WHEN THEY RECUR AND ARE METASTATIC, CAN EXPRESS NY-ESO ON THE ORDER OF ABOUT 30 PERCENT AS WELL. AND WE'VE ALSO SCREENED IT IN A NUMBER OF OTHER SOLID TUMORS. SO THAT'S WHY THE INDICATION IS, BROADLY SPEAKING, FOR SARCOMAS, BUT THE ACTUAL IND IS FOR ANY SOLID TUMOR. SO WE'RE ABLE TO CATCH A LOT OF OTHER MISCELLANEOUS TUMOR TYPES AS WELL.

CHAIRMAN THOMAS: THANK YOU.

MR. SHEEHY: ADDITIONAL QUESTIONS OR COMMENTS FROM THE BOARD? ANY OTHER PUBLIC COMMENT? THANK YOU. THEN COULD WE CALL THE ROLL 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: DAVE MARTIN.
DR. MARTIN: NO.
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, AS LONG AS I'M NOT IN CONFLICT. THE PI JUST MENTIONED THE UCLA/UCI ALPHA CLINIC. AND I DON'T RECALL SEEING THAT AS PART OF THE BUDGET. BUT AS LONG AS I'M NOT IN CONFLICT, YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.

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MR. TORRES: AYE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MS. BONNEVILLE: MOTION CARRIES.

MR. SHEEHY: THANK YOU. SO THAT CONCLUDES THE BUSINESS OF THE APPLICATION REVIEW SUBCOMMITTEE. CHAIRMAN THOMAS.

CHAIRMAN THOMAS: THANK YOU VERY MUCH, MR. SHEEHY.

DO WE HAVE ANY PUBLIC COMMENT AT ANY OF THE SITES ON ANY TOPIC THAT ANYBODY WISHES TO DISCUSS?

DR. NOWICKI: YES. I'M STILL HERE AT THE TABLE. THIS IS DR. NOWICKI. I JUST WANT TO THANK CIRM AND EVERYONE HERE ON BEHALF OF UCLA AND ON BEHALF OF OUR PATIENTS. THANK YOU.

DR. CHIU: ARLENE CHIU FROM THE CITY OF HOPE. I HAVE A QUICK QUESTION ABOUT THE SICKLE CELL INITIATIVE. IS THE INITIATIVE POSTED ANYWHERE THAT WE CAN SEE WHAT ARE THE CONDITIONS? THAT'S THE FIRST QUESTION.

AND THE SECOND QUESTION IS, HAVING SEEN THE RANGE OF SICKLE CELL FUNDING THAT CIRM HAS GIVEN OUT, WILL NHLBI BE HELPING OUT IN ANY OF THE OTHER CLINICAL TRIALS THAT ARE POSTED?

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DR. MILLAN: ARLENE, IT'S MARIA. I'M GOING TO HAVE GABE THOMPSON SUMMARIZE THE CONDITIONS OF THE MOU WITH THE NHLBI.

DR. CHIU: THANK YOU. IS THERE ALSO ANYTHING ON THE WEBSITE THAT I COULD REFER BACK TO IN CASE PEOPLE ARE INTERESTED OR NOT YET?

MR. THOMPSON: SO THE SICKLE CELL INITIATIVE IS ACTUALLY ON THE CIRM SITE. IT'S JUST GOING TO JUST COME THROUGH OUR REGULAR CLIN PROGRAM ANNOUNCEMENT, THE CLIN1, THE CLIN2, OR THE CLIN3.

THERE IS A UNIQUE APPLICATION THAT IS BUILT FOR THE INITIATIVE, AND I WILL SHARE WITH YOU THE LINK TO THE APPLICATION. BUT THEY WILL FOLLOW THE SAME PROGRAM ANNOUNCEMENT. SO THAT'S ALREADY POSTED.

DR. CHIU: THANK YOU.

MR. THOMPSON: TO ANSWER YOUR SECOND QUESTION, THE EXISTING AWARDS IN SICKLE CELL WOULDN'T NECESSARILY BE PART OF THIS INITIATIVE. ONLY NEW PROJECTS THAT COME IN FOR FUNDING.

DR. CHIU: GOT IT. THANK YOU.

MR. TORRES: YOU ALSO MAY KNOW THAT ASSEMBLY MEMBER MIKE GIPSON HAS A SICKLE CELL INITIATIVE FOR 15 MILLION IN THE LEGISLATURE, AND WE'RE MONITORING THAT LEGISLATION AS IT MOVES FROM

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ASSEMBLY AND HOPEFULLY TO THE SENATE.

DR. CHIU: THAT'S VERY EXCITING. THANK YOU VERY MUCH.

MR. TORRES: THAT'S AB1105.

CHAIRMAN THOMAS: ANY OTHER COMMENTS? HEARING NONE, THAT CONCLUDES TODAY'S AGENDA. I WOULD LIKE TO NOTE FOR MEMBERS OF THE BOARD USUALLY OUR NEXT IN-PERSON MEETING WOULD BE IN JUNE. HOWEVER, THIS YEAR, FOR SCHEDULING REASONS, THE NEXT IN-PERSON MEETING IS MAY 23D. WOULD ENCOURAGE EVERYBODY TO ATTEND IF AT ALL POSSIBLE. AND WITH THAT, THANK YOU, EVERYBODY, FOR YOUR ATTENDANCE AND PARTICIPATION. AND WE STAND ADJOURNED.

(THE MEETING WAS THEN CONCLUDED AT 1 P.M.)

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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 APRIL 29, 2019, 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
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