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

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: NOVEMBER 28, 2023
1 P.M.

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

FILE NO.: 2023-36

I N D E X

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

NOVEMBER 28, 2023; 1 P.M.

CHAIRMAN IMBASCIANI: GOOD AFTERNOON, EVERYONE. THE MEETING IS BEING RECORDED. THIS IS THE REGULAR MEETING OF THE APPLICATION REVIEW SUBCOMMITTEE OF THE CIRM BOARD. I WANT TO WELCOME EVERYONE ELECTRONICALLY ON ZOOM. I'M GOING TO ASK SCOT TO A TAKE A ROLL CALL AND FOR GIL TO CONDUCT THE MEETING. THANK YOU.

MR. TOCHER: DAN BERNAL. MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MR. TOCHER: JUDY CHOU.

DR. CHOU: PRESENT.

MR. TOCHER: LEONDRA CLARK-HARVEY.

MS. CLARK-HARVEY: PRESENT.

MR. TOCHER: ANNE-MARIE DULIEGE.

DR. DULIEGE: PRESENT.

MR. TOCHER: YSABEL DURON.

MS. DURON: HERE.

MR. TOCHER: MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: HERE.

MR. TOCHER: FRED FISHER.

DR. FISHER: PRESENT.

MR. TOCHER: ELENA FLOWERS.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DR. FLOWERS: PRESENT.

MR. TOCHER: DAVID HIGGINS.

DR. HIGGINS: HERE.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: HERE.

MR. TOCHER: RICH LAJARA.

MR. LAJARA: PRESENT.

MR. TOCHER: CHRISTINE MIASKOWSKI.

DR. MIASKOWSKI: PRESENT.

MR. TOCHER: LAUREN MILLER-ROGEN.

MS. MILLER-ROGEN: HERE.

MR. TOCHER: ADRIANA PADILLA.

DR. PADILLA: HERE.

MR. TOCHER: JOE PANETTA. MARVIN SOUTHARD.

DR. SOUTHARD: HERE.

MR. TOCHER: KAROL WATSON. KEVIN XU.

OKAY. WE HAVE A QUORUM.

CHAIRMAN IMBASCIANI: QUORUM IS GOOD. THANK YOU.

VICE CHAIR BONNEVILLE: YOU DID SOUND A LITTLE SURPRISED.

CHAIRMAN IMBASCIANI: I'M LOOKING AT THIS GALLERY VIEW OF SMILING FACES. ALL SET. IS THERE ANYTHING PRELIMINARY BEFORE WE START?

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

MR. TOCHER: WE CAN JUST TURN IT OVER TO GIL TO GET THE PRESENTATION.

CHAIRMAN IMBASCIANI: WE HAVE AN IMPOSING AGENDA OF FOUR APPLICATIONS TO REVIEW TODAY. GIL.

DR. SAMBRANO: THANK YOU. GOOD AFTERNOON, EVERYONE. SO TODAY DR. HAYLEY LAM AND MYSELF ARE GOING TO SPLIT THOSE FOUR AND PRESENT EACH OF US TWO APPLICATIONS TO YOU. THESE ARE THE RECOMMENDATIONS FROM THE GRANTS WORKING GROUP THAT ARE COMING FROM SEPTEMBER AND OCTOBER REVIEWS THAT WE HAD.

AND LET ME JUST GIVE YOU AN OVERVIEW TO GET US STARTED. AS ALWAYS, WE START WITH OUR MISSION, WHICH IS TO ACCELERATE WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO A DIVERSE CALIFORNIA AND WORLD.

AND WITH THAT, I WANT TO REMIND YOU OF THE BUDGET ALLOCATION THAT WE HAVE FOR THE CLINICAL PROGRAM AND SHOW YOU WHERE THE STATUS IS AS OF TODAY. SO WE HAD AN ALLOCATION OF 252 MILLION FOR CLIN PROGRAMS. THE AMOUNT THAT'S REQUESTED TODAY IS 18.5 MILLION. THE AMOUNT OF APPROVED AWARDS THAT WE'VE DONE THIS FISCAL YEAR SO FAR IS 62.1. SO IF YOU ARE TO APPROVE THE FOUR APPLICATIONS, THAT WOULD LEAVE US WITH 171 IN OUR POOL.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

THE SCIENTIFIC SCORING SYSTEM THAT'S USED BY THE GRANTS WORKING GROUP TO SCORE THESE APPLICATIONS IS A SYSTEM OF 1, 2, OR 3. A SCORE OF 1 MEANS THAT THE APPLICATION HAS EXCEPTIONAL MERIT AND WARRANTS FUNDING. THERE MAY BE SOME MINOR RECOMMENDATIONS THAT THEY MAKE, BUT THE GRANTS WORKING GROUP DOES NOT FEEL IT WARRANTS THEM LOOKING AT IT AGAIN. HOWEVER, A SCORE OF 2 IS ONE THAT NEEDS IMPROVEMENT. FOR THOSE WE PROVIDE COMMENTS BACK TO THE APPLICANTS. TYPICALLY THEY WILL REVISE THEIR APPLICATION AND RESUBMIT WITHIN A COUPLE MONTHS. AND THEN THOSE THAT RECEIVE A SCORE OF 3 ARE DEEMED TO BE SUFFICIENTLY FLAWED THAT THEY DO NOT WARRANT FUNDING AT THIS TIME.

THE SCIENTIFIC REVIEW CRITERIA THAT INFORMS THAT SCORE IS BASED ON THESE FIVE QUESTIONS. DOES THE PROJECT HOLD THE NECESSARY SIGNIFICANCE AND POTENTIAL FOR IMPACT? MEANING WHAT VALUE DOES IT OFFER AND IS IT SOMETHING THAT'S WORTH DOING. DOES IT HAVE A SOUND RATIONALE? IS IT WELL-PLANNED AND DESIGNED? AND IS IT FEASIBLE, INCLUDING HAVING THE APPROPRIATE TEAM ASSEMBLED TO CONDUCT THE WORK AS WELL AS HAVING APPROPRIATE RESOURCES TO DO THE WORK. AND THEN LASTLY, DOES THE PROJECT UPHOLD THE PRINCIPLES OF DIVERSITY, EQUITY, AND INCLUSION OR

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DEI?

IN ADDITION TO THE DEI THAT'S CONSIDERED BY THE SCIENTIFIC REVIEWERS, WE ALSO HAVE A SEPARATE DEI SCORE THAT IS GIVEN BY OUR PATIENT ADVOCATE MEMBERS OF THE BOARD. THE DEI SCORE SYSTEM IS 0 TO 10, WITH 10 BEING THE BEST POSSIBLE SCORE. AND THERE'S A RUBRIC THAT WE HAVE CREATED TO HELP INFORM HOW THE SCORING FOR THE DEI IS DONE. SO YOU WILL SEE TWO SCORES FOR EACH APPLICATION, ONE WITH THE OVERALL SCIENTIFIC SCORE AND THEN THE SEPARATE DEI SCORE.

THE COMPOSITION OF THE WORKING GROUP INCLUDES SCIENTIFIC MEMBERS WHO GIVE THAT SCIENTIFIC SCORE. THEY HAVE VARIED EXPERTISE THAT WE BRING TO THE TABLE IN ORDER TO ASSESS THESE APPLICATIONS. IN ADDITION TO THOSE 15 MEMBERS, WE HAVE SEVEN BOARD MEMBERS WHO ARE PATIENT ADVOCATE MEMBERS OF THE ICOC. THEY DO THE DEI EVALUATION, PROVIDE PATIENT PERSPECTIVE ON THE SIGNIFICANCE AND POTENTIAL FOR IMPACT, AND ALSO OVERSIGHT ON THE PROCESS. AND THEN ON OCCASION WE HAVE SCIENTIFIC SPECIALISTS WHO ARE NONVOTING MEMBERS. THEY PROVIDE A SCIENTIFIC EVALUATION IN AREAS WHERE WE HAVE GAPS OF KNOWLEDGE OR WHERE WE NEED TO BRING IN ADDITIONAL KNOWLEDGE RELATED TO ANY PARTICULAR AREA. AND FOR THOSE

MEMBERS, THEY DO NOT PROVIDE A FINAL SCIENTIFIC SCORE.

OKAY. SO WE'RE GOING TO TAKE EACH APPLICATION ONE AT A TIME. AND THE FIRST ONE HAS THE FOLLOWING CONFLICTS. SO JUST KEEP THIS IN MIND. WE'RE GOING TO SHOW YOU BEFORE EACH APPLICATION WHO MAY HAVE A CONFLICT WITH THAT APPLICATION. SO PLEASE REFRAIN FROM DISCUSSION OR MAKING COMMENTS RELATED TO THIS APPLICATION AS WE DISCUSS IT.

SO THIS IS CLIN1-14945. IT'S ENTITLED "PRECLINICAL TO CLINICAL GENE THERAPY DEVELOPMENT FOR CMT4J. THIS IS ADENOVIRUS 9 GENE THERAPY." THIS IS FOR PATIENTS THAT HAVE CMT4J, WHICH IS A MUTATION IN WHAT'S CALLED THE FIG4 GENE. I'LL TELL YOU A LITTLE BIT MORE ABOUT IT IN THE NEXT SLIDE. THE GOAL OF THIS STUDY IS TO COMPLETE PRE-IND ENABLING ACTIVITIES AND TO FILE AN IND. FUNDS REQUESTED ARE JUST UNDER 4 MILLION, AND THEY PROVIDE CO-FUNDING OF 982,000, WHICH IS THE 20 PERCENT THAT'S REQUIRED FOR THESE APPLICANTS.

ALL RIGHT. A LITTLE BACKGROUND ON THIS DISEASE. IT'S CHARCOT-MARIE-TOOTH DISEASE TYPE 4J IS THE FORMAL NAME, ABBREVIATED CMT4J. AND THIS AN ULTRA RARE DISEASE. IT IS DEBILITATING, PROGRESSIVE, HEREDITARY MOTOR AND SENSORY

NEUROLOGICAL DISEASE, AND IT'S CAUSED BY A HETEROALLELIC FIG4 GENE LOSS. AND THIS IS CHARACTERIZED BY PROGRESSIVE MOTOR WEAKNESS WITH SOME SENSORY INVOLVEMENT, RESULTING IN QUADRIPLEGIA, RESPIRATORY FAILURE, AND SHORTENED LIFESPAN. AND CURRENTLY THERE ARE NO TREATMENTS AVAILABLE TO SLOW OR HALT THE DISEASE PROGRESSION. IT IS SIMPLY READING THE SYMPTOMS AS BEST ONE CAN.

THE VALUE PROPOSITION FOR THIS THERAPY. THIS PROPOSED GENE THERAPY APPROACH UTILIZES AAV9 VECTOR TO TARGET AFFECTED NEURONS AND PROVIDE THAT MISSING FIG4 GENE. THE APPROACH HAS THE POTENTIAL TO SIGNIFICANTLY IMPROVE THE QUALITY OF LIFE FOR THOSE PATIENTS WHO ARE AFFECTED BY THIS DISEASE AND POSSIBLY HALT THE PROGRESSION OF THE DISEASE.

WHY IS THIS A STEM CELL OR GENE THERAPY? WELL, THIS IS A GENE THERAPY APPROACH THAT USES AAV9; THEREFORE, QUALIFIES FOR CIRM FUNDING.

THIS PARTICULAR DISEASE IS INDEED ULTRA RARE. AND SO IT IS NOT CURRENTLY REPRESENTED IN ANY OF OUR ACTIVE TRAN OR CLIN AWARDS. AND THIS PARTICULAR APPLICANT HAS NOT PREVIOUSLY RECEIVED A CIRM AWARD.

THE RECOMMENDATION FROM THE GRANTS WORKING GROUP INDICATES THAT THEY VOTED UNANIMOUSLY FOR A

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

SCORE OF 1 WITH 15 MEMBERS GIVING IT A SCORE OF 1. AND THE DEI MEDIAN SCORE WAS A 9. AND THE CIRM TEAM RECOMMENDATION IS TO FUND THIS APPLICATION FOR THE AWARD AMOUNT OF 3.93 MILLION. AND SO I TURN IT BACK TO YOU, MR. CHAIRMAN.

CHAIRMAN IMBASCIANI: LET'S START WITH COMMENTS -- CAN I BE HEARD?

MR. TOCHER: YEAH.

CHAIRMAN IMBASCIANI: START WITH COMMENTS FROM THE BOARD MEMBERS PLEASE.

DR. DULIEGE: I HAVE ONE QUESTION.

CHAIRMAN IMBASCIANI: ANNE-MARIE, PLEASE.

DR. DULIEGE: CAN YOU JUST TELL US WHAT IS THE ESTIMATED PREVALENCE OF THIS DISEASE IN CALIFORNIA? ROUGHLY HOW MANY PATIENTS MAY HAVE THIS PARTICULAR MUTATION?

DR. SAMBRANO: IT'S A GREAT QUESTION. IT'S HARD TO KNOW IN CALIFORNIA SPECIFICALLY. SO THE PREVALENCE IS ABOUT ONE IN A MILLION. SO IT IS AN ULTRA RARE INDICATION. THERE'S JUST OVER 30 PATIENTS THAT ARE PART OF THE GROUP THAT ARE KNOWN TO THE APPLICANTS THAT THEY WILL TAP INTO TO GATHER THOSE THAT WOULD PARTICIPATE IN THE FUTURE TRIAL THAT THEY'RE PREPARING FOR. AND THE FUTURE TRIAL WOULD ENROLL ABOUT 20 PATIENTS ULTIMATELY IF THEY

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

CAN MANAGE.

THEY ARE ALSO DOING A NATURAL HISTORY STUDY WHICH INCLUDES 20 PATIENTS THAT IS PART OF THIS GROUP. SO THE NUMBER OF PATIENTS IN CALIFORNIA, I DON'T HAVE THE INFORMATION OF PATIENTS KNOWN. IT IS SO RARE THAT -- I DON'T KNOW WHETHER THERE ARE ANY OR HOW MANY THERE WOULD BE IN CALIFORNIA.

DR. DULIEGE: I REALLY APPRECIATE THIS COMMENT, GIL. AND THE REASON FOR MY QUESTION IS CLEARLY BASED ON THE SCORING FROM THE GWG. IT'S SOMETHING THAT WE WOULD WANT TO FUND, THE FUND REQUEST. MY ONLY QUESTION IS WILL THE TEAM BE ABLE TO ENROLL 20 PATIENTS PLUS IN AN ACTUAL NATURAL HISTORY STUDY GIVEN HOW ULTRA RARE THAT IS? IS IT EVEN FEASIBLE?

DR. SAMBRANO: THAT'S ALSO A GREAT QUESTION. AND THEY HAVE ALREADY IDENTIFIED THE PATIENTS FOR THE NATURAL HISTORY STUDY. SO THEY HAVE THOSE ALREADY. SO I THINK THAT WAS PART OF THE CONFIDENCE THAT IT GAVE TO REVIEWERS OF THEM BEING ABLE TO ENROLL THE 20 THAT THEY NEED FOR THE ACTUAL CLINICAL STUDY ONCE THAT COMES INTO PLACE.

DR. DULIEGE: SO WITHOUT SPENDING TOO MUCH TIME ON THAT, I JUST WONDER IF THAT SHOULD BE TAKEN

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

INTO ACCOUNT IN OUR REASONING TO SUPPORT THE GRANT OR NOT, GIL OR OTHERS, WHICH IS NO QUESTION ABOUT THE SCIENCE AND THE JUDGMENT OF THE GWG. SHOULD WE FUND A TRIAL WHERE WE KNOW THAT THEY'RE GOING TO STRUGGLE ENORMOUSLY TO ENROLL THIS STUDY? AND PATIENTS EASILY PARTICIPATE IN A NATURAL HISTORY STUDY. IT'S ANOTHER STORY TO ENROLL IN A GENE THERAPY, EVEN IF THEIR GOAL FOR A BETTER LIFE IS DESPERATE.

SO I WELCOME YOUR OPINION, GIL OR ANYONE ELSE FOR THAT MATTER, HOW WE ARE SEEING THE TRIAL.

DR. CREASEY: MAY I SAY SOMETHING?

DR. DULIEGE: OF COURSE. I DIDN'T REALIZE YOU WERE HERE. SORRY ABOUT THAT.

DR. CREASEY: I WAS ON THE ZOOM ANYWAY. I'M SORRY, ANNE-MARIE. ACTUALLY THE INVESTIGATOR ALREADY LINED UP TWO, THREE PATIENTS TO COME TO CALIFORNIA OR ONE OF THEM IS IN CALIFORNIA. AND SO THEY'RE BRINGING THE PATIENTS TO CALIFORNIA FOR TREATMENT.

DR. DULIEGE: OKAY. SO YOU'RE CONFIDENT THEY CAN BRING A TOTAL OF 20 PATIENTS.

DR. CREASEY: WELL, NO. THEY'RE GOING TO TREAT AS GIL DESCRIBED. THEY WILL DO A NATURAL HISTORY STUDY, BUT THEY'RE GOING TO TREAT UP TO A

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

CERTAIN NUMBER, WHICH IS NOT ALL 20. REMEMBER THEY NEED TO IDENTIFY WITH A NATURAL PROGRESSION OF THE DISEASE SIMILAR TO A PLACEBO CONTROL. AND THEN ALSO TREAT UP TO MAYBE A MAXIMUM SIX OR MORE WITH THIS GENE THERAPY AS A COMPARATOR. SO THAT'S THE WAY IT WILL WORK.

DR. DULIEGE: GREAT. THANK YOU FOR THE CLARIFICATION.

DR. CREASEY: YOU'RE WELCOME.

CHAIRMAN IMBASCIANI: ANY OTHER BOARD MEMBERS HAVE COMMENTS?

VICE CHAIR BONNEVILLE: DAVID HIGGINS AND JUDY CHOU.

CHAIRMAN IMBASCIANI: DAVID HIGGINS IS NEXT.

DR. HIGGINS: I ASSUME THAT THESE RESEARCHERS WILL KNOW WHAT THEY'RE DOING MORE SO THAN EVEN WE DO. CAN YOU GO BACK TO THEM AND SAY, BECAUSE THIS IS SO RARE, YOU NEED TO ASK FOR MORE MONEY, OR WE NEED TO GIVE YOU MORE MONEY UP FRONT? AND IS IT TRUE THAT MORE MONEY EQUALS MORE PATIENTS, OR IS THAT A PIPE DREAM?

SO MY QUESTION IS SHOULD WE AS THE FUNDING AGENCY TELL THEM WHAT THEY NEED WHEN WE THINK THEY DON'T UNDERSTAND WHAT THEY NEED?

DR. SAMBRANO: THAT'S A GOOD QUESTION. I THINK PART OF THE ASSESSMENT OF THESE PROPOSALS INCLUDE WHAT THEIR ULTIMATE PLAN FOR ENROLLMENT AND RECRUITMENT OF THESE PATIENTS WOULD BE. SO THEY ADDRESS PART OF THAT IN HERE. JUST REMEMBERING THAT THIS IS CLIN1. THIS IS FOR THE IND-ENABLING WORK. THIS IS NOT YET FOR A CLINICAL TRIAL. SO THEY WOULD NOT DO THE CLINICAL TRIAL UNTIL THEY COMPLETE THESE INITIAL STUDIES.

BUT PART OF WHAT THEY DID THERE IN THE APPLICATION IS THEY'RE PARTNERED WITH A PATIENT ORGANIZATION. (INTERFERENCE.) ALL RIGHT. I'LL TRY AGAIN. THANK YOU.

SO THEY HAVE A PATIENT ADVOCACY ORGANIZATION THAT THEY HAVE PARTNERED WITH IN ORDER TO HELP IDENTIFY THESE PATIENTS. SO THERE IS A PLAN IN PLACE. SO THEY DO HAVE AN IDEA OF WHAT TO DO, BUT THEY DON'T HAVE TO DO IT AT THIS PARTICULAR STAGE.

DR. CHOU: I HAVE A FOLLOW-UP QUESTION. SO THEN IF I UNDERSTAND FROM ABLA'S RESPONSE, THE STUDY WILL BE DONE IN CALIFORNIA, OR THIS IS GOING TO BE A GLOBAL STUDY? AND THEN EVEN IF AT THIS STAGE, IT'S GOING TO BE STATE TREATED STUDY. REALISTICALLY MOVING FORWARD, DO THEY HAVE A PLAN

THAT THIS IS GOING TO BE A GLOBAL STUDY TO INCREASE THE NUMBER OF PATIENT TO BE ABLE TO DEMONSTRATE THE EFFICACY?

DR. SAMBRANO: RIGHT. SO THE COMPANY IS A CALIFORNIA ORGANIZATION. SO THEY HAVE A CLINICAL SITE IN CALIFORNIA AND ONE OUTSIDE OF CALIFORNIA THAT THEY WOULD PLAN TO USE AND PROBABLY WILL INCREASE THE NUMBER OF SITES BEYOND THAT. SO IT WOULD BE, IN TERMS OF THE PATIENT POPULATION THAT THEY WOULD RECRUIT, WOULD BE GLOBAL, BUT THERE'S GOING TO BE A LIMITED NUMBER OF SITES THAT INCLUDE CALIFORNIA.

DR. CHOU: I SEE.

DR. CREASEY: JUDY, IF I CAN SAY, THE ACTUAL APPLICANT ALREADY LINED UP ALL THOSE PATIENTS. IT'S SORT OF LIKE HE HAS BEEN PATIENT ADVOCATE ON BEHALF OF ALL THE FAMILIES THAT HAVE THOSE TYPES OF PATIENTS. SO ESSENTIALLY THE PATIENTS HAVE BEEN IDENTIFIED. AND IT'S ALMOST LIKE A CASE STUDY ON ITS OWN. THE PRINCIPAL CHAMPION OF THAT EFFORT WHO SET UP THE COMPANY CALLED OPEDA (PHONETIC) IN THE STATE OF CALIFORNIA IS WHO APPLIED ON BEHALF OF ALL THOSE FAMILIES.

DR. CHOU: SO MORE OR LESS THE BUDGET, INCLUDING TO BE ABLE TO FLY THE PATIENT TO THE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

STUDIES, ARE ALREADY INCLUDED?

DR. SAMBRANO: NO. BECAUSE THIS NOT FOR THE CLINICAL TRIAL. THIS IS FOR IND-ENABLING WORK. SO THE CLINICAL TRIAL IS NOT SOMETHING THAT WOULD BE FUNDED UNDER THIS AWARD.

DR. CHOU: THAT WILL BE THE NEXT STEP?

DR. SAMBRANO: CORRECT.

DR. CHOU: THANK YOU.

CHAIRMAN IMBASCIANI: I DON'T SEE ANY OTHER HANDS. DO WE HAVE PUBLIC COMMENT?

MR. TOCHER: WE DON'T HAVE A MOTION.

DR. FISHER: I MOVE TO APPROVE FUNDING FOR THIS.

DR. SOUTHARD: SECOND.

CHAIRMAN IMBASCIANI: FURTHER DISCUSSION FROM BOARD MEMBERS ON THE MOVEMENT TO ACCEPT 14945? IF NOT, PUBLIC COMMENT? DOES ANYONE SEE ANY?

MS. MANDAC: NO HANDS RAISED.

CHAIRMAN IMBASCIANI: SCOTT, I THINK WE CAN PROCEED THEN.

MR. TOCHER: JUDY CHOU.

DR. CHOU: AYE.

MR. TOCHER: LEONDRA CLARK-HARVEY. ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MR. TOCHER: MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: YES.

MR. TOCHER: FRED FISHER.

DR. FISHER: YES.

MR. TOCHER: ELENA FLOWERS.

DR. FLOWERS: YES.

MR. TOCHER: DAVID HIGGINS.

DR. HIGGINS: YES.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: YES.

MR. TOCHER: RICH LAJARA.

MR. LAJARA: YES.

MR. TOCHER: CHRISTINE MIASKOWSKI.

DR. MIASKOWSKI: YES.

MR. TOCHER: LAUREN MILLER-ROGEN.

MS. MILLER-ROGEN: YES.

MR. TOCHER: ADRIANA PADILLA.

DR. PADILLA: YES.

MR. TOCHER: JOE PANETTA.

MR. PANETTA: YES.

MR. TOCHER: MARVIN SOUTHARD.

DR. SOUTHARD: YES.

MR. TOCHER: KAROL WATSON.

ARE THERE ANY BOARD MEMBERS WHOSE NAMES I HAVE NOT CALLED WHO ARE NOT IN CONFLICT? GREAT.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

THANKS VERY MUCH. THE MOTION CARRIES.

CHAIRMAN IMBASCIANI: MOTION CARRIES. GOOD. THANK YOU. GIL, YOU MAY PROCEED.

DR. SAMBRANO: THANK YOU. SO THESE ARE THE CONFLICTS FOR THE NEXT APPLICATION. AND THE NEXT APPLICATION IS CLIN1-15060. THE TITLE IS "A 1XX-ENHANCED AND FULLY NONVIRAL BCMA CHIMERIC ANTIGEN RECEPTOR OR CAR-T CELL THERAPY FOR RELAPSED AND REFRACTORY MULTIPLE MYELOMA." THERAPY IS A CAR-T CRYOPRESERVED AUTOLOGOUS TRSC LOCUS BCMA-CAR-T CELLS. THE INDICATION IS, OF COURSE, FOR RELAPSED AND REFRACTORY MULTIPLE MYELOMA. AND THE GOAL IS, HERE ONCE AGAIN, TO COMPLETE IND-ENABLING STUDIES AND TO FILE AN IND FOR A FUTURE CLINICAL TRIAL. THE FUNDS REQUESTED ARE 4.585 MILLION. THERE IS NO CO-FUNDING REQUIRED FOR THIS APPLICANT.

A LITTLE BACKGROUND. MULTIPLE MYELOMA IS THE SECOND MOST COMMON MALIGNANCY AMONG BLOOD CANCERS AND PRIMARILY AFFECTS INDIVIDUALS THAT ARE OVER THE AGE OF 60, THE MEDIAN SURVIVAL BEING ABOUT SEVEN TO TEN YEARS. THERE ARE SEVERAL TREATMENTS THAT ARE AVAILABLE, BUT PATIENTS TYPICALLY WILL RELAPSE AND BECOME REFRACTORY TO ADDITIONAL LINES OF THERAPY. ON AVERAGE, A PATIENT WILL GO THROUGH FOUR TO FIVE DIFFERENT LINES OF THERAPY DURING THE COURSE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

OF MULTIPLE MYELOMA.

THE VALUE PROPOSITION FOR THIS PROPOSED THERAPY: CAR-T THERAPIES THAT TARGET BCMA HAVE DEMONSTRATED SIGNIFICANT PROMISE FOR TREATING RELAPSED AND REFRACTORY MULTIPLE MYELOMA, BUT THE CURRENT APPROACHES STILL HAVE LIMITATIONS. ONE OF THOSE IS PARTICULARLY THE RELAPSE THAT OFTEN OCCURS AND THE PROPOSED THERAPY NEEDED TO OVERCOME THESE LIMITATIONS AND PRODUCE A CAR-T THERAPY THAT WOULD BE MORE PERSISTENT AND REDUCE RELAPSE. IT ALSO OFFERS THE POSSIBILITY OF MAKING THE MANUFACTURING OF THE THERAPY MORE EFFICIENT AND LESS EXPENSIVE.

AND SO WHY IS THIS A STEM CELL OR GENE THERAPY? THIS IS A THERAPY THAT'S COMPOSED OF T-MEMORY STEM CELLS. IT IS ALSO A THERAPY THAT WOULD BE CONSIDERED A GENE THERAPY BECAUSE OF THE GENETIC MANIPULATION IN CREATING THE CAR-T.

THIS PARTICULAR -- WELL, WE CURRENTLY DON'T HAVE ANY ACTIVE TRAN OR CLIN PROJECTS IN MULTIPLE MYELOMA AT THIS TIME. WE HAVE HAD SOME VERY EARLY IN THE DISCOVERY STAGE AND HAVE HAD SOME IN THE PAST THAT WERE LATER STAGE.

THIS APPLICANT HAS NOT PREVIOUSLY RECEIVED A CIRM AWARD. HERE'S THE RECOMMENDATION FROM THE GRANTS WORKING GROUP. THE GRANTS WORKING GROUP

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

MEMBERS VOTED WITH 11 MEMBERS GIVING THIS A SCORE OF 1, THERE WERE THREE THAT GAVE IT A SCORE OF 2, AND THE DEI WAS A SCORE OF 9. THE CIRM TEAM RECOMMENDATION IS TO FUND IN THE AMOUNT OF 4.585 MILLION. BACK TO YOU, MR. CHAIRMAN.

CHAIRMAN IMBASCIANI: THANK YOU, GIL. HAVING HEARD THE PRESENTATION ON 15060, THE CHAIR WILL ENTERTAIN A MOTION.

DR. SOUTHARD: MOVE APPROVAL.

CHAIRMAN IMBASCIANI: MARVIN MOVES.

DR. HIGGINS: SECOND.

CHAIRMAN IMBASCIANI: MOTION IS MOVED AND SECONDED. WE CAN START WITH DISCUSSION FROM THE BOARD MEMBERS.

MR. TOCHER: I DON'T SEE ANY HANDS.

CHAIRMAN IMBASCIANI: I DON'T SEE ANY HANDS. I'LL GIVE IT FIVE SECONDS. OKAY. CAN YOU CHECK FOR PUBLIC COMMENT AT THIS POINT?

MS. MANDAC: NO HANDS.

CHAIRMAN IMBASCIANI: NOT SEEING ANYTHING. ALL RIGHT. I THINK WE CAN PROCEED, SCOTT, WITH OUR VOTE.

MR. TOCHER: THE MOTION IS TO FUND CLIN1-15060.

JUDY CHOU.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DR. CHOU: YES.

MR. TOCHER: LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: YES.

MR. TOCHER: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MR. TOCHER: YSABEL DURON.

MS. DURON: YES.

MR. TOCHER: MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: YES.

MR. TOCHER: FRED FISHER.

DR. FISHER: YES.

MR. TOCHER: DAVID HIGGINS.

DR. HIGGINS: YES.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: YES.

MR. TOCHER: STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

MR. TOCHER: RICH LAJARA.

MR. LAJARA: YES.

MR. TOCHER: LAUREN MILLER-ROGEN.

MS. MILLER-ROGEN: YES.

MR. TOCHER: ADRIANA PADILLA.

DR. PADILLA: YES.

MR. TOCHER: JOE PANETTA.

MR. PANETTA: YES.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

MR. TOCHER: MARVIN SOUTHARD.

DR. SOUTHARD: YES.

MR. TOCHER: KAROL WATSON.

THE MOTION CARRIES.

CHAIRMAN IMBASCIANI: MOTION CARRIES. VERY NICE. GIL, WOULD YOU TAKE US INTO THE THIRD APPLICATION.

DR. SAMBRANO: DR. HAYLEY LAM IS GOING TO PRESENT THE LAST TWO.

DR. LAM: GOOD AFTERNOON, EVERYONE. SO THE THIRD APPLICATION IS CLIN2-15085. THIS IS A PERSONALIZED ANTISENSE OLIGONUCLEOTIDE THERAPY FOR A RARE PEDIATRIC GENETIC DISEASE: SCN2A. SO THE TITLE IS, I THINK, SOMEWHAT SELF-EXPLANATORY. THIS IS A THERAPY THAT'S A PERSONALIZED ANTISENSE OLIGONUCLEOTIDE DRUG, AND THE INDICATION IS SCN2A-ASSOCIATED GENETIC DISORDER.

THE GOAL OF THE PROJECT IS TO COMPLETE A FIRST-IN-HUMAN TRIAL, AND THEY'RE REQUESTING JUST UNDER ONE MILLION IN FUNDING WITH NO CO-FUNDING REQUIRED AND NONE PROVIDED.

A LITTLE BIT OF BACKGROUND ON THIS. SO THE DISORDERS ARE NAMED AS SUCH BECAUSE THEY ARE MUTATIONS ESSENTIALLY IN THE SCN2A GENE. AND SO THE CLASS OF DISORDERS RESULTS IN KIND OF A RANGE OF

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

NEURODEVELOPMENTAL CONDITIONS AND MAINLY ARE CHARACTERIZED BY HOW SEVERE THE EPILEPSY IS. THAT'S A SIDE EFFECT OF IT. THE SEVERE FORMS OF THIS DISEASE CAUSE SEIZURES BEGINNING IN INFANCY, AND COMMONLY THE TYPICAL ANTISEIZURE MEDICATIONS ARE NOT EFFECTIVE.

SO THE PROPOSED THERAPY WOULD TREAT A SINGLE PATIENT WITH SEVERE EPILEPSY AND SEVERE NEURODEVELOPMENTAL DELAY. IF IT'S SUCCESSFUL, OTHER PEOPLE WITH SIMILAR DISORDERS COULD POTENTIALLY BENEFIT FROM EQUIVALENT PRECISION THERAPIES. AND THIS IS A GENE THERAPY PRODUCT.

CIRM DOES NOT CURRENTLY FUND ANY ACTIVE TRAN OR CLIN AWARDS FOR THIS DISORDER.

AND THE APPLICANT HAS RECEIVED PRIOR CIRM FUNDING WITH AN ACTIVE DISCOVERY STAGE AWARD. THIS IS CANDIDATE DISCOVERY EARLIER STAGE, AND IT'S ABOUT HALFWAY THROUGH RIGHT NOW.

AND FINALLY, THE GRANTS WORKING GROUP RECOMMENDATION WAS A TIER I TO RECOMMEND FOR FUNDING AND THE DEI SCORE OF 8.5. AND THE CIRM TEAM CONCURS WITH THE GRANTS WORKING GROUP FOR THE AWARD AMOUNT OF JUST UNDER ONE MILLION. BACK TO THE CHAIR.

CHAIRMAN IMBASCIANI: THANK YOU. I WOULD LIKE TO HAVE A MOTION TO CONSIDER THIS APPLICATION.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

YSABEL, YOU WANTED TO SPEAK?

MS. DURON: I WAS GOING TO ASK A QUESTION, BUT DO WE WAIT FOR THE MOTION FIRST?

CHAIRMAN IMBASCIANI: YOU CAN DO BOTH.

MS. DURON: LET ME ASK THE QUESTION FIRST THEN. GIVEN SIX WERE A 2, CAN YOU DESCRIBE, EITHER GIL OR HAYLEY, WHAT THE HESITATION WAS? IT SEEMS HIGH, BUT SIX STILL WASN'T TOP OF THE LINE. WHAT WERE THE HESITATIONS?

DR. LAM: SO THE MAIN CONCERNS OF THE PANEL WERE AROUND THE MONITORING OF THE SUBJECT AFTER TREATMENT. SO THE CLINICIANS WANTED THERE TO BE EEG MONITORING OF THE SEIZURES POST-TREATMENT BECAUSE THEY FELT IT WOULD BE MORE ACCURATE. THE CURRENT PROTOCOL ASKS FOR SORT OF PARENT-REPORTED SEIZURES, WHICH THE PANEL THOUGHT MAY OR MAY NOT BE ACCURATE BECAUSE PARENTS ARE NOT NECESSARILY WITH THE PERSON ALL THE TIME AND MAYBE CAN MISIDENTIFY, THAT SORT OF THING. SO THEY WANTED THE APPLICANT TO REVISE THE EEG MONITORING FROM -- I THINK THEY HAVE ONE TIME PLANNED AT 12 MONTHS, SO THEY WANTED A COUPLE OF ADDITIONAL TIME POINTS ADDED.

MS. DURON: I DON'T RECALL THE DEI SCORE. CAN REMIND ME WHAT THAT WAS?

DR. LAM: YES. I BELIEVE IT WAS 8.5.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

MS. DURON: SO WE KNOW THAT THIS IS A PROBLEM THAT EXISTS ACROSS RACIAL/ETHNIC GROUPS?

DR. LAM: I THINK -- SO ACCORDING TO THE APPLICANT, THEY'VE ONLY HAD NINE CASES IDENTIFIED WITH THIS GENETIC DISORDER. SO I'M NOT SURE IF THERE'S ENOUGH DATA ON THAT.

MS. DURON: CONSIDERED RARE. I'M WONDERING HOW THEY GOT AN 8.5 IF THE RESEARCHERS THEMSELVES CAN'T IDENTIFY THAT THERE'S A RACIAL/ETHNIC ISSUE INVOLVED HERE OR THIS IS SPECIFIC TO ONE GROUP OR A SPECIFIC GROUP OF CHILDREN. HOW DO YOU GET AN 8.5 IF THEY DON'T KNOW?

DR. SAMBRANO: YSABEL, I THINK THE PROBLEM IS THAT IT'S SO RARE, WITH LESS THAN TEN PATIENTS WORLDWIDE, THAT IT WOULD BE HARD TO KNOW WHETHER IT IMPACTS A DIVERSE POPULATION OR NOT. JUST BASED ON TEN PATIENTS, THEY CAN GIVE YOU NUMBERS THERE OR THEY CAN GIVE YOU A DISTRIBUTION OF WHAT MAY EXIST THERE, BUT IT'S NOT GOING TO BE PREDICTIVE OF WHAT MAY EXIST WORLDWIDE.

MS. DURON: BUT NOBODY ASKED ABOUT THE DIFFERENT PATIENTS OR THE BREAKDOWN OF JUST THOSE TEN TO KNOW THAT THERE WAS SOME DIVERSE. I KNOW YOU TALK ABOUT RARITY, BUT I'M CURIOUS HOW YOU GET SUCH A HIGH SCORE WHEN YOU DON'T HAVE THE DATA TO

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

SUBSTANTIATE OR NOT THAT THEY IN FACT HAVE THE DIVERSE -- A DEI PLAN THAT THEY UNDERSTAND. I'M CONFUSING MYSELF.

DR. LAM: I THINK I WOULD -- JUST TO -- IF YOU LOOK AT THE COMMENTS, I THINK, FROM THE DEI SECTIONS, THAT THE APPLICANT INSTITUTION HAS A STRONG DEI TRACK RECORD, AND THEY HAVE LANGUAGE SUPPORT FOR THE VARIOUS POSSIBLE PATIENTS THAT THEY COULD POTENTIALLY DRAW UPON. AND SO IT WAS, I THINK, WITH THE CAVEAT, I THINK THE PANEL UNDERSTOOD THAT THIS WAS VERY RARE. AND THAT THERE WAS ONE COMMENT, THAT THE IDENTIFICATION OF THE DISEASE MEANS THAT THERE HAS TO BE GENETIC TESTING. AND SO THAT DOES HAVE A COST ASSOCIATED WITH IT.

MS. DURON: THAT SHOULDN'T LEAVE PEOPLE OUT BECAUSE THEY CAN'T AFFORD THE COST. I'M A SHADE CONFUSED HERE.

CHAIRMAN IMBASCIANI: LET ME ASK AGAIN FOR A MOTION TO CONSIDER.

MR. JUELSGAARD: I THINK THERE ARE MORE QUESTIONS THAN THERE ARE READY FOR A MOTION JUST YET.

CHAIRMAN IMBASCIANI: ANNE-MARIE, YOU HAVE A QUESTION?

DR. DULIEGE: I ASSUME THAT WE SHOULD VOTE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

ON WHETHER WE APPROVE THE ADDITIONAL FUNDING FOR THE STUDY AND WE SHOULD NOT QUESTION THE ORIGINAL IDEA OF THE STUDY; IS THAT RIGHT? IS THAT CORRECT?

DR. SAMBRANO: I'M SORRY. COULD YOU REPEAT THAT?

DR. DULIEGE: I JUST WANT TO CLARIFY WHAT WE ARE VOTING ON, AND I'M PRETTY SURE. BUT I ASSUME WE ARE VOTING FOR ALLOWING ADDITIONAL FUNDS TO THE TUNE OF LESS THAN $1 MILLION TO BE GIVEN TO FINISH THE TRIAL. WE ARE NOT VOTING, NOR EVEN QUESTIONING THE ORIGINAL FUNDING OF THE TRIAL; IS THAT RIGHT? IT'S A SUPPLEMENTAL FUNDING.

DR. LAM: NO, NO. THIS IS A FIRST-IN-HUMAN TRIAL THAT'S GOING TO TREAT ONE PATIENT.

DR. DULIEGE: I SEE. THE N EQUALS 1.

DR. LAM: CORRECT.

DR. DULIEGE: THANK YOU. SO IT'S THE ORIGINAL TRIAL AND THE COST IS CLOSE TO $1 MILLION FOR THIS PARTICULAR PATIENT?

DR. SAMBRANO: CORRECT.

DR. LAM: YES.

DR. DULIEGE: SO THEN MY QUESTION BECOMES MORE RELEVANT AND VALID, WHICH IS I DON'T KNOW OF ANY INTERVENTION THAT CAN TACKLE A DEVELOPMENTAL

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DELAY WHEN IT HAS ALREADY HAPPENED. AT BEST YOU CAN PREVENT PROGRESSIONAL DEVELOPMENT DELAY. I DON'T THINK YOU CAN EVER REVERSE ONE. MAYBE I'M WRONG. SO IS THERE A VALUE, AND IT'S NOT THE AMOUNT OF MONEY BECAUSE, OF COURSE, RELATIVELY SPEAKING, COMPARED TO THE REST OF THE GRANTS WE ARE MAKING, THIS IS RATHER SMALL, BUT IS THERE VALUE IN SPENDING MONEY ON SOMETHING I DON'T BELIEVE CAN BE ACHIEVED? IT WOULD BE A TOTALLY DIFFERENT SITUATION IF THE INDICATION WAS SEVERE INTRACTABLE SEIZURES WITH THE GOAL OF PREVENTING DEVELOPMENTAL DELAY, BUT I DON'T THINK THAT'S WHAT I'VE HEARD. AND I HAVE A QUESTION ABOUT THAT, TO MY KNOWLEDGE, AND I'D LOVE TO BE TOLD AGAIN THAT I MAY NOT KNOW IT SO WELL, CANNOT BE ACHIEVED.

DR. LAM: SO THERE WAS SOME DISCUSSION AMONGST THE PANEL ON THIS ISSUE, AND IT'S BASICALLY UNKNOWN. THEY DON'T EXPECT THERE TO BE RECOVERY OF NEURODEVELOPMENTAL DELAY THAT'S ALREADY HAPPENED, BUT THEY DO BELIEVE IT'S POSSIBLE THAT THE EPILEPTIC EPISODES CAN BE REDUCED; SO, THEREFORE, COULD HAVE BENEFIT IN THAT SENSE. THAT COMMENT CAME FROM ONE OF THE --

DR. DULIEGE: I WONDER IF OTHERS AND YOU, GIL, CAN COMMENT YOUR OPINION ON THAT BECAUSE THERE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

ARE THINGS WE KNOW AND THINGS WE DON'T KNOW, BUT THERE ARE LOTS OF THINGS WE DON'T KNOW. I BELIEVE THAT IF YOU STOP A PROCESS SUCH AS INTRACTABLE SEIZURE, YOU CAN STOP THE PROGRESSION OF DEVELOPMENTAL DELAY. I'VE NEVER HEARD REALLY AT ALL A SITUATION WHERE YOU CAN REVERSE DEVELOPMENT DELAY. PARTICULARLY IN CHILDREN, I DON'T KNOW THE AGE AND I DON'T KNOW ALSO THE SERIOUSNESS OF THAT PARTICULAR PERSON'S DEVELOPMENT DELAY. I JUST HAVE A LITTLE PROBLEM OF VOTING MONEY FOR SOMETHING THAT ISN'T DOABLE; HOWEVER, THE ENDPOINT OF INTRACTABLE SEIZURE IS A MORE DOABLE ENDPOINT.

CHAIRMAN IMBASCIANI: STEVE, YOUR HAND IS UP.

MR. JUELSGAARD: YES. I'M GOING TO -- ACTUALLY THIS DOVETAILS A LITTLE BIT WITH YSABEL'S QUESTION, BUT IT REALLY IS A DIFFERENT POINT. THIS IS A STUDY, JUST TO BE VERY CLEAR, THIS IS A STUDY IN ONLY ONE PERSON WITH AN EXTREMELY RARE DISEASE. THERE ARE -- IF YOU READ THE WHOLE REVIEW THAT THE GWG PROVIDED, THERE HAVE BEEN ONLY NINE PEOPLE IDENTIFIED IN THE WHOLE WORLD WITH THIS CONDITION. SO EXTREMELY, EXTREMELY RARE.

SO NOW THIS IS NEW GROUND AS FAR AS I'M CONCERNED FOR US. SO WE ARE GETTING INTO THE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

BUSINESS OF PROVIDING POTENTIAL TREATMENT FOR ONE PERSON FOR A DISEASE THAT HARDLY EVER OCCURS. AND THE QUESTION GETS TO BE, IF THIS WORKS, ARE WE NOW BOUND TO PROVIDE SUPPORT FOR THIS PERSON FOR THE REST OF THEIR LIFE? I'M GOING TO ASSUME THAT THEY'RE NOT GOING TO BE ABLE TO FIND VERY MANY OTHER PEOPLE AROUND TO BE TREATED. WE'RE TALKING ON A GLOBAL BASIS ONLY NINE OR TEN PEOPLE LIKE THIS. AND THIS IS SOMETHING THAT WE SHOULD BE DOING.

I DON'T KNOW THAT I HAVE AN ANSWER TO THAT, BUT WE ARE GETTING OURSELVES REALLY INTO THE QUESTIONS OF THESE VERY, VERY RARE DISEASES, WHAT ROLE ARE WE GOING TO BE PLAYING. AND I UNDERSTAND THIS IS A REALLY DIFFICULT DISEASE PARTICULARLY FOR THE FAMILY OF THIS PATIENT; BUT ON THE OTHER HAND, WE ARE NOW POTENTIALLY LINING OURSELVES UP TO BECOME THE PAYERS. AND IF CIRM ULTIMATELY IS NOT GETTING FUNDED AGAIN IN THE FUTURE, THE PARENTS ARE GOING TO BE IN A POSITION OF TRYING TO FIGURE OUT HOW TO PAY FOR THIS THERAPY BECAUSE I DON'T KNOW THAT INSURANCE WILL EVER PAY FOR IT.

I'M A LITTLE BIT TROUBLED BY THIS, AND I THINK IT'S WORTH THINKING ABOUT A LITTLE BIT, JUST THE NATURE OF THIS DISEASE AND THE RARITY OF IT AND WHAT THINGS LOOK LIKE DOWN THE ROAD.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DR. LAM: CAN I JUST SPEAK TO THAT BRIEFLY? I CAN'T ANSWER THE QUESTION ABOUT WHETHER IT SHOULD BE FUNDED OR NOT FOR THIS PARTICULAR AWARD. BUT THIS IS FOR THE TRIAL OF A SINGLE PATIENT, AND THERE IS A FOUNDATION THAT'S PARTNERING WITH THE APPLICANT THAT HAS, AT LEAST IN THE LETTER OF SUPPORT, HAS COMMITTED TO PROVIDE THE TREATMENT TO THE PATIENT FOR THEIR LIFETIME.

MR. JUELSGAARD: THAT'S HELPFUL. I DIDN'T SEE THAT ANYWHERE.

CHAIRMAN IMBASCIANI: THANK YOU, STEVE, FOR THOSE IMPORTANT COMMENTS AND FOR HAYLEY. I'M GOING TO GO TO MARIA AND THEN FRED FISHER.

VICE CHAIR BONNEVILLE: I HAVE SIMILAR COMMENTS THAT STEVE HAD. I ALSO, JUST FROM A PHILOSOPHICAL PERSPECTIVE, IS CIRM GOING TO CONTINUE TO FUND APPLICATIONS THAT COME IN THAT TREAT A SINGLE PATIENT? AND THAT CALLS INTO QUESTION WHETHER HOW QUICKLY WE CAN GET A STRATEGY AROUND A RARE DISEASE, HOW WE FUND RARE DISEASE, WHERE IT'S GOING, AND HOW BENEFITS CAN BE SHOWN TO HELP IN OTHER DISEASE INDICATIONS BECAUSE OFTENTIMES THAT IS THE CASE.

SO IT PUTS US INTO -- IT SETS A PRECEDENT FOR US IF WE FUND THIS. IT'S MERITORIOUS, WHAT DO

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

WE DO IN THE FUTURE? I'M NOT SUGGESTING WE SHOULDN'T FUND IT. IT'S JUST A PHILOSOPHICAL QUESTION, AND I THINK THAT'S SOMETHING THAT THE BOARD ALONG WITH THE INTERNAL TEAM NEED TO HAVE A DISCUSSION AROUND AT SOME POINT.

CHAIRMAN IMBASCIANI: FRED.

DR. FISHER: SO THIS IS A VERY INTERESTING DISCUSSION, BUT I WOULD SUGGEST THIS IS NOT THE PLACE FOR THE DISCUSSION THAT'S HAPPENING. WE'VE SPENT AN INORDINATE AMOUNT OF TIME TALKING ABOUT SOMETHING THAT IS NOT THE PURVIEW OF THIS COMMITTEE. ALTHOUGH I AGREE THAT STEVE AND MARIA HAVE PROPOSED SUBSTANTIVE TOPICS THAT THE BOARD MIGHT CHOOSE TO CHEW ON AT A BOARD MEETING WHERE THIS ISSUE IS AGENDIZED BECAUSE WHERE THE LINE IS DRAWN BETWEEN RARE DISEASE, ULTRA RARE, EXTREMELY RARE, N OF 1, THESE ARE DISTINCTIONS THAT ARE NOT NECESSARILY CLEAR IN EVERYONE'S MIND AND CERTAINLY ARE NOT GROUNDED IN POLICY.

SO LET'S TAKE THIS CONVERSATION TO THE POLICY PLACE, WHICH IS THE BOARD, I THINK. LET'S FOCUS ON THIS APPLICATION, WHICH GOT EIGHT OF THE SCIENTISTS SAYING THIS IS A GREAT IDEA, LET'S DO IT, AND SIX SAYING THIS IS A REALLY GOOD IDEA, BUT NEEDS A LITTLE TWEAKING HERE AND THERE IN THEIR MINDS TO

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

GET IT FUNDABLE. AND MY GUESS IS THE CIRM STAFF ARE COMPLETELY CAPABLE OF ADDRESSING THE ISSUES THAT WERE IDENTIFIED BY THE SIX IN ORDER TO SATISFY ANYONE WHO HAS CONCERNS THAT THE VOTE WAS DIVIDED EIGHT TO SIX.

I WOULD BE SAYING SOMETHING COMPLETELY DIFFERENT IF IT WAS DIVIDED EIGHT TO SIX WITH THE SIX BEING THREE AND THE EIGHT BEING ONE. SO WE DON'T EVEN HAVE A MOTION ON THE TABLE, WHICH I THINK SHOULD ACTUALLY PRECEDE THESE KINDS OF DISCUSSIONS RATHER THAN COME AFTER THE FACT. THAT'S AGAIN, ANOTHER THING THAT'S UP TO THE CHAIR TO DECIDE. BUT LET'S JUST FOCUS ON THIS APPLICATION AND CONSIDER THE MERITS OF THIS APPLICATION. THANK YOU.

CHAIRMAN IMBASCIANI: LEONDRA, BEFORE I GET TO YOU, LET ME MAKE A COMMENT. FIRST OF ALL, FRED, I TRIED TO GET A MOTION. I AGREE WITH YOU. I THINK THIS IS A DISCUSSION OF THE MOTION.

NO. 2, I LIKE YOUR SUGGESTION, THAT THIS SHOULD BE CHEWED OVER, I THINK THOSE ARE YOUR WORDS, BY THE ENTIRE BOARD. SO I THINK I WILL ASK THE SCIENCE SUBCOMMITTEE TO BRING THIS ISSUE TO THE BOARD FOR A FULL DISCUSSION THAT'S DULY AGENDIZED. THANK YOU FOR THAT.

LEONDRA.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DR. CLARK-HARVEY: I WAS JUST GOING TO SUPPORT THAT AS WELL. I DO FEEL -- I FEEL UNCOMFORTABLE VOTING BECAUSE I KNOW WHAT OUR MISSION IS, BUT THIS IS REALLY A QUESTION AROUND HOW DO WE ENACT THAT IN THIS CASE. AND I DO FEEL THAT WE NEED TO BE CLEAR AND LEVEL SET WITH THE GREATER BOARD, AS FRED HAS SUGGESTED AND OTHERS, AROUND WHAT THAT LOOKS LIKE FOR US BECAUSE THIS MAY COME UP IN THE FUTURE, AND I'M NOT COMFORTABLE SETTING A PRECEDENT IN THIS MEETING.

CHAIRMAN IMBASCIANI: THANK YOU. I'M GOING TO ASK OUR BOARD COUNSEL HERE A QUESTION NOW. IF NO MOTION COMES TO ACCEPT THIS, DOES THIS GO INTO A LIMBO FOR FUTURE DISCUSSION MAYBE AFTER THE BOARD HAS A DEEPER CONVERSATION ON THIS TOPIC?

MR. TOCHER: YOU COULD TABLE CONSIDERATION OF THIS UNTIL SUCH TIME AS THE LARGER CONVERSATION HAPPENS IF THERE IS NO MOTION. TYPICALLY WE WOULD -- IF THERE IS NO MOTION TO FUND, WE WOULD ENTERTAIN A MOTION NOT TO FUND. BUT IT'S UP TO YOU.

CHAIRMAN IMBASCIANI: I LIKE THAT SUGGESTION. MAYBE THE BOARD MEMBERS HEARD THAT. IF SOMEBODY WOULD LIKE TO TABLE A DECISION ON THIS APPLICATION TO A DATE CERTAIN -- TO A DATE UNCERTAIN, BUT NOT TO BE FORGOTTEN.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DR. DULIEGE: I'M HAPPY TO ENTERTAIN THAT MOTION, THAT A DECISION ON THIS PARTICULAR APPLICATION SHOULD BE TABLED UNTIL THE BOARD HAS A CHANCE TO REVIEW THE ENTIRE PHILOSOPHY AROUND ULTRA RARE DISEASE.

CHAIRMAN IMBASCIANI: THANK YOU, ANNE-MARIE. WE HAVE A MOTION.

DR. FISHER: SECOND.

CHAIRMAN IMBASCIANI: SECONDED BY FRED.

I'M A LITTLE RUSTY ON ROBERTS RULES. A MOTION TO TABLE, DOES THAT HAVE TO BE VOTED ON?

MR. TOCHER: YOU CAN ASK IF THERE IS ANY OBJECTION TO TABLING THE MATTER.

CHAIRMAN IMBASCIANI: THANK YOU. YOU HEARD BOARD COUNSEL. IS THERE ANY OBJECTION TO OUR TABLING THIS ISSUE? THANK YOU SO MUCH. OKAY. GOOD. WE HAVE TABLED IT.

GIL, I'M GOING TO ASK YOU THEN TO GO ON TO THE FOURTH AND LAST APPLICATION.

DR. LAM: SO THERE'S ONE CONFLICT ON THIS APPLICATION. AND THE APPLICATION IS CLIN2-15115. THE CURE TRIAL: CELLULAR THERAPY FOR IN UTERO REPAIR OF MYELOMENINGOCELE -- I CAN'T SAY IT. IT'S ESSENTIALLY SPINA BIFIDA. AND SO THE THERAPY IS ALLOGENEIC MESENCHYMAL STEM CELLS ON A MATRIX GRAFT.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

AND THE GOAL IS TO COMPLETE A PHASE 2A CLINICAL TRIAL. THE FUNDS REQUESTED ARE JUST UNDER 9 MILLION, AND THE APPLICANT HAS PROVIDED JUST UNDER 6 MILLION OF THE CO-FUNDING, WHICH IS 40 PERCENT REQUIRED.

SO A LITTLE BIT OF BACKGROUND. SO THIS IS A BIRTH DEFECT THAT OCCURS WITH AN INCOMPLETE CLOSURE OF THE SPINAL CORD WHILE IT'S DEVELOPING AND RESULTS IN DAMAGE TO THAT EXPOSED SPINAL CORD. AND THE DAMAGE LEADS TO LIFELONG LOWER BODY PARALYSIS AND BLADDER AND BOWEL DYSFUNCTION IF NOT TREATED.

SO THE CURRENT STANDARD OF CARE IS IN UTERO SURGERY WHICH IMPROVES THE QUALITY OF LIFE OF CHILDREN BORN WITH THIS CONDITION, BUT OVER HALF STILL CANNOT WALK INDEPENDENTLY.

SO THE VALUE PROPOSITION OF THE PROPOSED THERAPY IS THAT IT COULD IMPROVE THE MOTOR OUTCOMES OF THE CHILDREN BORN WITH THIS CONDITION COMPARED TO SURGERY ALONE AND ULTIMATELY, IF SUCCESSFUL, WOULD RESULT IN MORE CHILDREN WHO ARE ABLE TO WALK.

AND THIS PROJECT IS COMPOSED PARTLY OF MESENCHYMAL STEM CELLS TOGETHER WITH A MATRIX MATERIAL.

SIMILAR CIRM PORTFOLIO PROJECTS: THERE'S ESSENTIALLY THE PHASE 1 PART OF THIS CURRENT

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

APPLICATION UNDER YOUR CONSIDERATION THAT IS FINISHING UP. AND THIS IS FOR THE SAME PRODUCT FOR THE SAME INDICATION.

AND THE PRIOR CIRM FUNDING TO THE APPLICANT TEAM, ESSENTIALLY THIS PARTICULAR PROJECT HAS BEEN FUNDED BY CIRM SINCE THE PRECLINICAL STAGE AND HAS PROGRESSED TO WHAT YOU'RE CONSIDERING TODAY.

AND THE GRANTS WORKING GROUP IS A UNANIMOUS RECOMMENDATION FOR FUNDING OF A TIER I, A DEI SCORE OF 9, AND A CIRM TEAM RECOMMENDATION TO FUND AS WELL FOR, AGAIN, THE TOTAL AMOUNT OF JUST UNDER NINE MILLION.

CHAIRMAN IMBASCIANI: THAT'S IT, HAYLEY? THANK YOU. OKAY.

DR. LAM: THAT'S IT FOR ME. THANK YOU.

CHAIRMAN IMBASCIANI: WE HAVE A MOTION TO CONSIDER DISCUSSION OF THIS FINAL APPLICATION.

VICE CHAIR BONNEVILLE: SO MOVED.

CHAIRMAN IMBASCIANI: MARIA BONNEVILLE HAS MOVED. DO I HEAR A SECOND?

DR. FLOWERS: SECOND.

CHAIRMAN IMBASCIANI: ELENA, THANK YOU, RIGHT HERE IN THE ROOM.

BOARD MEMBERS, COMMENTS ON THIS IN UTERO SURGERY FOR SPINA BIFIDA? OKAY. ANY MEMBERS OF THE

PUBLIC WANT TO CHIME IN? DO YOU SEE ANYTHING? NOTHING? OKAY. NOTHING. SCOTT, READY FOR THE VOTE.

MR. TOCHER: THE MOTION IS TO FUND CLIN2-15115.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

MR. TOCHER: JUDY CHOU.

DR. CHOU: YES.

MR. TOCHER: LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: YES.

MR. TOCHER: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MR. TOCHER: MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: YES.

MR. TOCHER: FRED FISHER.

DR. FISHER: YES.

MR. TOCHER: ELENA FLOWERS.

DR. FLOWERS: YES.

MR. TOCHER: DAVID HIGGINS.

DR. HIGGINS: YES.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: YES.

MR. TOCHER: STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

MR. TOCHER: RICH LAJARA.

MR. LAJARA: YES.

MR. TOCHER: CHRISTINE MIASKOWSKI.

DR. MIASKOWSKI: YES.

MR. TOCHER: LAUREN MILLER-ROGEN.

MS. MILLER-ROGEN: YES.

MR. TOCHER: ADRIANA PADILLA.

DR. PADILLA: YES.

MR. TOCHER: JOE PANETTA.

MR. PANETTA: YES.

MR. TOCHER: MARVIN SOUTHARD.

DR. SOUTHARD: YES.

MR. TOCHER: GREAT. THANKS VERY MUCH. AND THE MOTION CARRIES.

CHAIRMAN IMBASCIANI: GIL OR HAYLEY, ANY FINAL REMARKS?

DR. SAMBRANO: NO. THANK YOU VERY MUCH FOR YOUR TIME AND YOUR DISCUSSION. THANK YOU.

CHAIRMAN IMBASCIANI: OKAY. WORK FOR THE CHAIR IS TO ASSIGN THE TOPIC OF THE TREATMENT OF N OF 1 APPLICATIONS TO COME TO THE BOARD VIA THE SCIENCE SUBCOMMITTEE.

WITH THAT, I KNOW WE'RE GOING TO HAVE ONE MORE BOARD MEETING IN DECEMBER, BUT THIS COMMITTEE WILL NOT MEET AGAIN UNTIL THE NEW YEAR. SO IF I

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

DON'T SEE ANY OF YOU ON THE SUBCOMMITTEE BEFORE 2024, HAPPY HOLIDAYS TO ALL.

(THE MEETING WAS THEN CONCLUDED AT 1:53 P.M.)

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-920-3543 DRAIBE@HOTMAIL.COM

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 VIRTUAL PROCEEDINGS BEFORE THE APPLICATION REVIEW SUBCOMMITTEE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON NOVEMBER 28, 2023, 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, CA CSR 7152
133 HENNA COURT
SANDPOINT, IDAHO
(208) 920-3543