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 21, 2024
9 A.M.

REPORTER: BETH C. DRAIN, CA CSR
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I N D E X

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NOVEMBER 21, 2024; 9 A.M.

CHAIRMAN IMBASCIANI: SCOTT, IT'S MY PLEASURE TO CALL TO ORDER --

MR. TOCHER: HOLD ONE SECOND. HAVE WE STARTED THE ZOOM, THE YOUTUBE?

MS. MANDAC: YES.

MR. TOCHER: OKAY.

CHAIRMAN IMBASCIANI: OKAY. I'M GOING TO CALL TO ORDER NOW THE IF THE 58TH MEETING OF THE APPLICATION REVIEW SUBCOMMITTEE. AND I'M GOING TO ASK SCOTT TO START BY TAKING THE ROLL.

MR. TOCHER: THANK YOU, VITO.

DAN BERNAL.

MR. BERNAL: PRESENT.

MR. TOCHER: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: HERE.

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

DR. DULIEGE: HERE.

MR. TOCHER: YSABEL DURON.

MS. DURON: HERE.

MR. TOCHER: MARK FISCHER-COLBRIE.

MR. FISCHER-COLBRIE: HERE.

MR. TOCHER: ELENA FLOWERS.

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DR. FLOWERS: PRESENT.
MR. TOCHER: DAVID HIGGINS. VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: HERE.
MR. TOCHER: RICH LAJARA.
MR. LAJARA: HERE.
MR. TOCHER: CHRIS MIASKOWSKI.
DR. MIASKOWSKI: PRESENT.
MR. TOCHER: LAUREN MILLER-ROGEN.
DR. MILLAN: HERE.
MR. TOCHER: ADRIANA PADILLA.
DR. PADILLA: HERE.
MR. TOCHER: JOE PANETTA.
MR. PANETTA: HERE.
MR. TOCHER: MARV SOUTHARD.
DR. SOUTHARD: HERE.
MR. TOCHER: KAROL WATSON.
DR. WATSON: HERE.
MR. TOCHER: KEVIN XU.
MS. MANDAC: ACTUALLY JUST JOINING.
MR. TOCHER: OKAY. I SEE THAT CONCERN`KEVIN IS JUST JOINING US.
DR. XU: HERE. SORRY.
MR. TOCHER: GREAT. THANK YOU, KEVIN. OKAY. WE'RE GOOD TO GO, VITO. WE HAVE A QUORUM.

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CHAIRMAN IMBASCIANI: THANK YOU, SCOTT.

SO WE'RE GOING TO CONSIDER THE APPLICATIONS SUBMITTED IN RESPONSE TO CLINICAL STAGE PROJECTS IN THE PROGRAM ANNOUNCEMENT. AND DR. HAYLEY LAM IS GOING TO MAKE THE PRESENTATION OF THE APPLICATIONS. TAKE IT AWAY, HAYLEY.

DR. LAM: THANK YOU. GOOD MORNING TO THE BOARD. CAN YOU ALL SEE MY SHARED SCREEN?

MS. MANDAC: YEP.

DR. LAM: GREAT. THANK YOU.

SO I'LL BE TAKING YOU THROUGH THE CLINICAL APPLICATIONS TODAY. AS ALWAYS, WE BEGIN WITH OUR MISSION: ACCELERATING WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO A DIVERSE CALIFORNIA AND WORLD.

THE CURRENT BUDGET STATUS FOR THE CLINICAL PROGRAM IS AS FOLLOWS: 145.5 WAS APPROVED OR ALLOCATED, RATHER, TO THE CLINICAL BUDGET, AND 14 MILLION HAS BEEN APPROVED SO FAR. AND THERE'S JUST UNDER 30 MILLION UP FOR DISCUSSION TODAY.

THE SCORING SYSTEM FOR THE CLINICAL PROGRAM REMAINS AS A 1, 2, AND A 3. A 1 IS A RECOMMENDATION FOR FUNDING, WHICH ARE THE APPLICATIONS BEFORE YOU TODAY. A 2, THE APPLICANT

CAN IMPROVE THE PROJECT AND DOES NOT WARRANT FUNDING AT THIS TIME, BUT THEY CAN RETURN WITH A REVISION SUBMISSION. A SCORE OF A 3 IS A DO NOT RECOMMEND FOR FUNDING, AND THE SAME PROJECT CANNOT RETURN FOR AT LEAST SIX MONTHS.

THE REVIEW CRITERIA BY WHICH THESE APPLICATIONS ARE SCORED FOR THE SCIENTIFIC ASPECTS ARE THESE FIVE. SO DOES THE PROJECT HOLD THE NECESSARY SIGNIFICANCE AND POTENTIAL FOR IMPACT? IS THE RATIONALE SOUND? IS THE PROJECT WELL-PLANNED AND DESIGNED? IS THE PROJECT FEASIBLE? AND DOES THE PROJECT UPHOLD PRINCIPLES OF DIVERSITY, EQUITY, AND INCLUSION?

IN OUR CLINICAL PROGRAM, IN ADDITION TO THE SCIENTIFIC SCORING, WE ALSO HAVE A DIVERSITY, EQUITY, AND INCLUSION SCORING, WHICH IS A SCALE OF ZERO TO TEN, WITH TEN BEING AN OUTSTANDING RESPONSE. AND THESE ARE SCORED BY ALL MEMBERS OF THE GRANTS WORKING GROUP BOARD MEMBERS WITH NO CONFLICT.

THE REVIEW PANEL THAT REVIEWS ALL OF THESE APPLICATIONS IS COMPOSED AS FOLLOWS. THERE'S UP TO 15 SCIENTIFIC GROUP MEMBERS, AND THESE FOLKS PROVIDE THE SCIENTIFIC EVALUATION ACROSS THE DISEASE AREA, MANUFACTURING, REGULATORY, PRODUCT DEVELOPMENT THAT PROVIDE THE SCIENTIFIC SCORE FOR ALL APPLICATIONS.

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OUR GRANTS WORKING GROUP BOARD MEMBERS, WHICH IS OUR PATIENT ADVOCATE AND NURSE MEMBERS OF THE BOARD, WHICH CONDUCT A DEI EVALUATION AND PROVIDE A PATIENT PERSPECTIVE ON THE APPLICATIONS. AND THEY PROVIDE A DEI SCORE ON ALL APPLICATIONS, AND THEY'RE ALSO INVITED TO SUGGEST A SCIENTIFIC SCORE.

IN ADDITION, WE HAVE NONVOTING SCIENTIFIC SPECIALISTS THAT WE BRING IN, AS NEEDED, TO PROVIDE EXPERTISE IN AREAS THAT ARE NOT COVERED BY OUR PANELISTS, OUR SCIENTIFIC GRANTS WORKING GROUP MEMBERS.

SO WITH THAT, I'LL BE GOING STRAIGHT INTO THE APPLICATIONS. THE FIRST APPLICATION FOR THE COMMITTEE TO CONSIDER IS CLIN2-17078. SO THIS IS A GENE-EDITED STEM CELL PRODUCT FOR ADA-SCID, WHICH I'LL TALK ABOUT A LITTLE BIT MORE. THE GOAL OF THIS PROJECT IS TO ESTABLISH COMMERCIAL MANUFACTURING OF THE PRODUCT IN ANTICIPATION OF FILING FOR LICENSING OF THE PRODUCT. THEY'RE REQUESTING JUST UNDER 15 MILLION WITH JUST UNDER 10 MILLION IN CO-FUNDING, AND THIS IS A CALIFORNIA ORGANIZATION.

SO A LITTLE BIT ABOUT THE DISEASE. SO ADA-SCID IS AN ADENOSINE DEAMINASE DEFICIENCY. ESSENTIALLY THESE PATIENTS HAVE A NONFUNCTIONING IMMUNE SYSTEM; AND IF IT'S NOT TREATED, IT'S

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GENERALLY FATAL WITHIN THE FIRST TWO YEARS OF LIFE.

THE CURRENT TREATMENT THAT'S IDEAL IS A MATCH-RELATED SIBLING DONOR TRANSPLANT. AND IT USUALLY IS QUITE SUCCESSFUL, BUT IT'S ONLY AVAILABLE FOR ABOUT 20 PERCENT OF PATIENTS.

SO THE PROPOSED THERAPY FOR FOLKS THAT DON'T HAVE AN IDEAL DONOR, THERE IS SIGNIFICANT RISKS OF REJECTION AND LONG-TERM SIDE EFFECTS OF THE TREATMENT FROM A TRANSPLANT. AND THE PROPOSED THERAPY IS ESSENTIALLY TO CORRECT THE PATIENT'S OWN COPY OF THAT ADA ENZYME. AND IT'S A POTENTIALLY A CURATIVE TREATMENT THAT IS A ONE-TIME TREATMENT AND HAS LOWER REJECTION RISKS AND LOWER RISK OF LONG-TERM SIDE EFFECTS.

AND HOW IT'S RELEVANT TO CIRM IS THAT IT'S A GENE-EDITED STEM CELL PRODUCT.

IN TERMS OF THE CIRM PORTFOLIO, THERE IS A CURRENT RUNNING PHASE 2 TRIAL FOR THE SAME PRODUCT. THIS TRIAL HAS BEEN ONGOING FOR A WHILE, BUT STILL HAS SOME FUNDING IN IT AND IS ANTICIPATED TO BE ABLE TO TREAT A FEW MORE PATIENTS WITH THE REMAINING FUNDS.

THE APPLICANT TEAM HAS RECEIVED SEVERAL APPLICATION OR SEVERAL AWARDS, RATHER, FROM CIRM PREVIOUSLY. SOME OF THEM ARE ACTIVE AWARDS ACROSS

ALL THE SPECTRUM ESSENTIALLY OF OUR PRODUCT DEVELOPMENT PIPELINE. SO TRANSLATIONAL AND DISCOVERY AND AS WELL AS SOME AWARDS THAT HAVE BEEN CLOSED. AND ALL OF THESE APPROACHES ARE SIMILAR IN THE SENSE THAT THEY ARE GENE CORRECTING THE PATIENT'S OWN CELLS FOR A GENE THAT HAS A MUTATION IN IT.

SO FOR YOUR CONSIDERATION TODAY IS THIS APPLICATION YOU'VE BEEN DISCUSSING, EFFICACY AND SAFETY OF CRYOPRESERVED AUTOLOGOUS CD34+HSC TRANSDUCED WITH EFS-ADA LENTIVIRAL VECTOR ENCODING FOR THE HUMAN ADA GENE IN ADA-SCID SUBJECTS. AND SO THEY'RE REQUESTING 14.798 MILLION, AND THE GWG RECOMMENDATION FOR THIS WAS A UNANIMOUS 15 VOTES IN FAVOR OF FUNDING, AND A DEI SCORE OF 8.5, AND THE CIRM TEAM CONCURS WITH THE RECOMMENDATION OF THE GRANTS WORKING GROUP. THANK YOU.

CHAIRMAN IMBASCIANI: THANK YOU, HAYLEY. CHAIR WOULD LIKE TO ENTERTAIN A MOTION TO ACCEPT THE RECOMMENDATION ON THIS APPLICATION.

DR. DULIEGE: I MOVE.

DR. SOUTHARD: AND MARV SECONDS.

CHAIRMAN IMBASCIANI: ANNE-MARIE AND --

MR. TOCHER: MARV SOUTHARD.

CHAIRMAN IMBASCIANI: THANK YOU, MARVIN.

OKAY. THE FLOOR IS OPEN FOR DISCUSSION BY BOARD MEMBERS ON APPLICATION 17078.

MS. MANDAC: MARIA HAS HER HAND UP.

CHAIRMAN IMBASCIANI: YOU CAN SEE THAT BETTER THAN I. THANK YOU. MARIA.

VICE CHAIR BONNEVILLE: HI. I JUST HAVE A QUESTION FOR THE TEAM. SO THIS IS AN AWARD THAT WE CURRENTLY FUND, AND THIS IS JUST TO EXTEND THE WORK ALREADY BEING DONE TO BE ABLE TO TREAT MORE PATIENTS WITHIN THE SAME TRIAL IT? IS THAT WHAT I'M UNDERSTANDING?

DR. LAM: SO THE PURPOSE OF THIS PROJECT IS TO FUND THE COMMERCIAL MANUFACTURING OF THE PRODUCT. SO -- AND THAT'S A NECESSARY STEP TO BE ABLE TO FILE FOR THE BLA FOR LICENSING IF THAT MAKES SENSE.

VICE CHAIR BONNEVILLE: AND IN ORDER TO DO THAT, WE NEEDED TO ADD -- THEY NEEDED TO ADD MORE PEOPLE -- MORE TRIAL PARTICIPANTS?

DR. LAM: CORRECT. SO THE --

VICE CHAIR BONNEVILLE: GO AHEAD.

DR. LAM: YES. SO THE FDA IS REQUESTING FOR THE COMMERCIAL PRODUCT THAT THEY HAVE ESSENTIALLY PROOF THAT THAT COMMERCIAL PRODUCT IS EQUIVALENT TO WHAT THEY'VE BEEN USING.

VICE CHAIR BONNEVILLE: IS THAT AN ACTIVITY THAT WE NORMALLY FUND, OR IS THIS SOMETHING THAT -- HAVE WE DONE THIS BEFORE IS, I GUESS, MY QUESTION. AND IS THIS A NECESSARY -- IT IS SOMETHING WE ANTICIPATE WE WILL BE DOING FOR OTHER AWARDS IN ORDER TO GET THEM TO A BLA?

DR. LAM: YES. SO IT WOULD BE AN EXPECTED STEP FOR BLA.

VICE CHAIR BONNEVILLE: THANK YOU.

MS. DURON: SORRY. MY RAISED HAND DOESN'T WORK. SORRY, VITO.

WHEN WE TALKED ABOUT GETTING IT TO MARKET OR TO MANUFACTURE IT, REMIND ME, ONE, IF WE GET ANY DOLLARS BACK ONCE IT GETS INTO MANUFACTURING. AND, TWO, DO WE HAVE SOME CONTROL OR SAY OVER PRICING WHICH OFTENTIMES IN THE VERY RARE DISEASES USUALLY IS A REALLY BIG LIFT FOR MOST FAMILIES? SO I'M WONDERING WHERE WE COME IN ON THAT AND WHAT WE CAN SAY ABOUT THAT.

DR. LAM: ABOUT YOUR FIRST QUESTION, I'M NOT EXACTLY SURE WHAT -- CAN YOU CLARIFY ON THE MANUFACTURING?

MS. DURON: IT'S MY UNDERSTANDING, BASED ON WHAT MARIA JUST SAID -- JUST ASKED, THAT IT IS LEADING TOWARDS MANUFACTURING. IT'S STILL IN TRIAL.

I'M ASSUMING THAT BECAUSE I KNOW WE TALKED ABOUT GETTING INTO SUPPORTING BUILDING MANUFACTURING AND WORKING WITH MANUFACTURING. SO I'M JUST -- I'M ASSUMING WE'RE MOVING IN THAT DIRECTION TO GET OKAY. AND IF I'M WRONG, PLEASE CLEAR IT UP FOR ME. BUT I'M ACTUALLY MORE CONCERNED ABOUT PRICING AND IMPACT OF THIS AND WHAT KIND OF SAY WE HAVE IN REGULATING PRICING.

DR. SAMBRANO: HAYLEY, YOU WANT ME TO RESPOND?

DR. LAM: SURE.

DR. SAMBRANO: YEAH. JUST TO CLARIFY, THESE APPLICANTS ARE IN THEIR LAST STEPS TOWARDS GETTING A BLA. IF THEY DO, AND THEY WOULDN'T NECESSARILY ACHIEVE THAT UNTIL THE END OF THIS AWARD, THEY NEED TO CONDUCT THESE MANUFACTURING ACTIVITIES TO GET TO THAT PLACE. ONCE THEY DO GET A BLA AND BEGIN COMMERCIALIZATION ACTIVITIES, THEN THERE ARE THE REGULATIONS THAT WE HAVE IN PLACE THAT WOULD APPLY IN TERMS OF THE RELATIVE AMOUNT THAT WE PROVIDE TO HOW MUCH THEY MAKE OR IF THEY CHOOSE TO LICENSE THE PRODUCT AND SO ON. SO THOSE RULES WILL -- PROBABLY SCOTT AND RAFAEL KNOW WAY BETTER THAN I DO. BUT THOSE DON'T APPLY UNTIL THEY COMPLETE THOSE ACTIVITIES AND GET TO THIS POINT.

BUT THE ACTIVITIES THAT WE WOULD BE FUNDING UNDER THIS AWARD ARE CONSISTENT WITH THE TYPES OF ACTIVITIES THAT WE HAVE FUNDED FOR OTHER PROJECTS. I THINK HERE WE'RE LOOKING AT THE VERY TAIL END OF WHAT WOULD BE THE EQUIVALENT OF A PHASE 3 AND INTO BLA.

MS. DURON: SO I'M GOING TO BE STUPID AGAIN, GIL, AND ASK ANOTHER QUESTION --

DR. SAMBRANO: NO WORRIES.

MS. DURON: -- BECAUSE I'M STILL VERY -- WHAT I REALLY WANT TO KNOW IS AT WHAT POINT, AT ANY POINT IN TIME DO WE HAVE A SAY. IF IT GETS INTO MANUFACTURING AND COMMERCIALIZATION, DO WE HAVE ANY SAY ON PRICING OR CONTROL BECAUSE THIS IS THE KIND OF, YOU KNOW, IF IT'S A RARE DISEASE AND IT IS AN INVALUABLE DISCOVERY, IT'S GOING TO BE VERY PRICEY. AND MY CONCERN IS THAT A LOT OF THOSE CHILDREN WHO SUFFER FROM IT, THEIR FAMILIES DON'T NECESSARILY HAVE A TON OF MONEY TO AFFORD IT, AFFORD THIS CURE I WOULD HOPE IT'S CALLED. SO I'M JUST WONDERING IF WE, CIRM, HAVE -- AND MAYBE J.T. CAN ANSWER. BUT I'M JUST KIND OF WONDERING NOW AS WE KEEP TALKING ABOUT COMMERCIALIZATION AND WHO KNOWS WHAT'S GOING TO HAPPEN IN THE CONTEXT OF OUR NEXT ADMINISTRATION. SO I'M -- I'M JUST WONDERING IF WE

HAVE ANY POWER, SINCE WE FUNDED THINGS LIKE THIS, THAT WE CAN HELP KEEP THE COST DOWN.

MR. TOCHER: VITO, THIS IS SCOTT. IF I CAN JUMP IN PERHAPS.

CHAIRMAN IMBASCIANI: BECAUSE I HAVE FOUR PEOPLE WITH THEIR HANDS UP, BUT I WANT SOMEONE OUT OF ORDER EVEN WHO WILL RESPOND TO THAT QUESTION. IS THAT YOU, SCOTT?

MR. TOCHER: THAT'S RIGHT.

CHAIRMAN IMBASCIANI: GO AHEAD.

MR. TOCHER: YSABEL, I DON'T WANT TO -- CAN YOU HEAR ME, YSABEL?

MS. DURON: YES, SCOTT, I CAN.

MR. TOCHER: OKAY. THANK YOU. AND I DON'T WANT TO OVERWHELM EVERYONE WITH A PRIMER IN OUR IP REGS, BUT YOUR QUESTION IS A GREAT ONE AND ONE THAT THE INSTITUTE HAS WRESTLED WITH FOR MANY YEARS AND HAS DEVELOPED A POLICY THAT'S EMBODIED IN OUR INTELLECTUAL PROPERTY REGULATIONS. AND THAT PROVIDES, PURSUANT TO PROP 14 -- 71'S MANDATE, THAT CALIFORNIANS WITH NO OTHER MEANS HAVE ACCESS TO THERAPIES THAT ARE DEVELOPED WITH CIRM FUNDING.

SO TO YOUR QUESTION, CALIFORNIANS WHO FALL UNDER 300 PERCENT OF THE FEDERAL POVERTY LINE, A COMMERCIALIZING ENTITY MUST COME WITH AN ACCESS PLAN

AND PRESENT THAT PLAN TO THIS BOARD FOR APPROVAL THAT WILL ADDRESS ACCESS TO SUCH CALIFORNIANS. AND THE BOARD HAS AN UP-OR-DOWN VOTE ON THAT.

IN ADDITION, CALIFORNIA PUBLIC ENTITIES THAT PURCHASE WITH PUBLIC FUNDS ALSO MUST BE PROVIDED ACCESS AND PRICING THAT IS NEGOTIATED WITH THOSE ENTITIES AT A DISCOUNT.

AND THEN FINALLY, THERE IS A THIRD LEG. AND, OF COURSE, NATURALLY I'M FORGETTING IT. WE HAVE THE ACCESS PLANS AND THEN CALIFORNIA PRICING. OH, THAT'S RIGHT. AND THIS IS A VESTIGE OF AN EARLIER LAW IN CALIFORNIA, I BELIEVE IT WAS UNDER THE SCHWARZENEGGER ADMINISTRATION, THAT THE CALIFORNIA DISCOUNT PRESCRIPTION DRUG PROGRAM, THE CDPDP, WHICH WAS NEVER FUNDED UNFORTUNATELY, WAS A STATEWIDE, AS IT MAY IMPLY, DISCOUNT PRESCRIPTION DRUG PROGRAM.

SO WHAT WE'VE SAID IS WE'VE SORT OF BOOTSTRAPPED TO THAT BODY OF LAW BASICALLY SAID WHENEVER THIS PROGRAM GOES LIVE OR IT'S SUCCESSOR GOES LIVE, THEN A COMMERCIALIZING ENTITY MUST PARTICIPATE IN THAT PROGRAM TO PROVIDE DISCOUNTED PRESCRIPTION DRUGS TO CALIFORNIANS.

SO THOSE ARE SORT OF THE THREE PRICING LEGS OF THE STOOL THAT CALIFORNIA HAS FOR

COMMERCIALIZING ENTITIES. THANK YOU, VITO.

CHAIRMAN IMBASCIANI: THANKS. SO I HAVE ANNE-MARIE AND MARIA. WHICH OF YOU WANTS TO FOLLOW ON TO THIS DISCUSSION? ANNE-MARIE.

DR. DULIEGE: OKAY. DOESN'T MATTER. IT'S NOT DIRECTLY RELATED ALTHOUGH I UNDERSTAND THE IMPORTANCE OF THE QUESTION YSABEL WAS ASKING. JUST TO CLARIFY AND FOLLOW UP TO MARIA'S FIRST QUESTION. THIS PROJECT HAS ALREADY BEEN FUNDED. IT'S IN PHASE 2. AND I WOULD BE CURIOUS TO KNOW HOW MANY PATIENTS HAVE BEEN ENROLLED OUT OF HOW MANY PATIENTS SHOULD BE ENROLLED JUST TO KNOW WHERE WE ARE.

BUT THEN THIS -- IS THIS TO ADD PATIENTS WITH A NEW MARKET COMMERCIAL LEVEL MANUFACTURING PROCESS TO SHOW TO THE FDA THAT THE RESULTS WERE SIMILAR WITH THE UPDATED MANUFACTURING PROCESS?

DR. LAM: YES.

DR. DULIEGE: OR ARE THESE PURELY MANUFACTURING ACTIVITIES?

DR. LAM: NO. THEY WOULD HAVE TO MAN- -- THE FUNDING IS TO MANUFACTURE THE COMMERCIAL PRODUCT AND THEN TREAT PATIENTS AND DEMONSTRATE, HOPEFULLY, IDEALLY, THAT THE TREATMENT HAS SIMILAR RESULTS IN THOSE TRIAL PARTICIPANTS.

DR. DULIEGE: SO THIS IS A SECOND STEP,

MANUFACTURING, WHICH IS PARALLEL TO THE ONGOING PHASE 2 TRIAL. AND THEN WHEN THE MANUFACTURING IS AVAILABLE, MORE PATIENTS WILL THEN BE ADDED WHICH MAY REQUIRE MORE FUNDING.

DR. LAM: CORRECT. I MEAN -- RIGHT. SO THE -- RIGHT.

DR. DULIEGE: BRIEFLY, I DO UNDERSTAND HOW THINGS HAPPEN IN CLINICAL DEVELOPMENT AND IT TAKES SUCH A HUGE AMOUNT OF TIME THAT WE GO IN PARALLEL RATHER THAN IN SEQUENTIAL STEPS. IT WOULD HAVE BEEN IDEAL, BUT I THINK JUST SHARING MY KNOWLEDGE HERE TO FIRST HAVE A KNOWLEDGE THAT THIS INTERVENTION IS EFFECTIVE AND THEN DO THE MANUFACTURING PROCESS. BUT I BELIEVE THAT IN REALITY IT WOULD BE -- IT'S A RISK TAKING, BUT PATIENTS CANNOT AFFORD THAT WE TAKE SO MUCH TIME IN THE DEVELOPMENT. I ASSUME THAT THAT'S THE REALITY. THANK YOU.

DR. LAM: YEAH. WELL, I MEAN I WILL SAY I BELIEVE THAT THIS GROUP HAS TREATED, I THINK, IT'S OVER 50 PATIENTS WITH THE PRODUCT, WITH THE NONCOMMERCIAL PRODUCT. AND THEY HAD REALLY, I MEAN AS FAR AS I'M CONCERNED, PRETTY GOOD RESULTS, I THINK.

DR. DULIEGE: GREAT.

DR. LAM: SO IF THEY PUBLISHED, I THINK

LIKE THE MOST RECENT ONE I THINK WAS THE PUBLICATION WHERE 48 OF THE 50 PATIENTS ACHIEVED LONG-TERM IMMUNE RESTORATION.

DR. DULIEGE: GREAT. WELL, VERY USEFUL INFORMATION. THANK YOU.

DR. LAM: SO I THINK -- YEAH.

CHAIRMAN IMBASCIANI: THANK YOU, HAYLEY, FOR THE CLARIFYING COMMENTS. I SAW SOME HANDS GO DOWN, BUT I WANT TO OFFER THE OPPORTUNITY IF RAFAEL OR MARIA OR ANYONE ELSE TO ADD ANYTHING AT THIS POINT.

MR. AGUIRRE-SACASA: NOTHING FROM ME. SCOTT DID A GREAT JOB.

CHAIRMAN IMBASCIANI: OKAY. THANK YOU, RAFAEL. ANY OTHER COMMENTS FROM BOARD MEMBERS ON 17078?

DR. LAM: DR. IMBASCIANI, IF I MAY, I ALSO JUST WANTED TO ADD A COMMENT RELATED TO THIS PARTICULAR APPLICATION WITH REGARDS TO, I THINK, YSABEL'S QUESTIONS.

CHAIRMAN IMBASCIANI: PLEASE DO.

DR. LAM: THIS PARTICULAR APPLICANT IS WORKING WITH A PUBLIC BENEFIT CORPORATION AND THE COMMERCIAL MANUFACTURING PARTNER. AND THIS PARTICULAR PARTNERSHIP, THEY ARE -- ONE OF THEIR

MAIN FOCUSES, THE INTENT IS, AT LEAST, TO BE PATIENT FOCUSED IN TERMS OF ACCESS TO THIS THERAPY.

CHAIRMAN IMBASCIANI: UH-HUH.

MS. DURON: THANK YOU, HAYLEY. MAY I JUST SAY THIS KIND OF COSTS, EVEN WITH HELP, CAN SOMETIMES BREAK THE BACK OF EVEN MIDDLE INCOME FAMILIES AND EVEN UPPER INCOME FAMILIES. SO I'M JUST -- I WAS JUST WONDERING ABOUT IT. BUT THANKS, EVERYBODY, FOR THE CLARIFICATIONS. I APPRECIATE IT.

CHAIRMAN IMBASCIANI: OKAY, YSABEL. I DON'T SEE ANY OTHER COMMENT. I'LL ASK IF THERE'S ANY MEMBER OF THE PUBLIC THAT WOULD LIKE TO COMMENT ON THIS APPLICATION.

MS. MANDAC: THERE ARE NO HANDS RAISED.

CHAIRMAN IMBASCIANI: THERE ARE NO HANDS RAISED. SCOTT, I THINK WE ARE READY TO GO TO A ROLL CALL VOTE.

MR. TOCHER: GREAT. AND THE MOTION IS TO FUND CLIN2-17078.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

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

DR. DULIEGE: YES.

MR. TOCHER: YSABEL DURON.

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MS. DURON: YES.
MR. TOCHER: MARK FISCHER-COLBRIE.
MR. FISCHER-COLBRIE: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: 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.
MR. TOCHER: MARV SOUTHARD.
DR. SOUTHARD: YES.
MR. TOCHER: KEVIN XU.
DR. XU: YES.
MR. TOCHER: THANK YOU VERY MUCH. THE MOTION CARRIES.
CHAIRMAN IMBASCIANI: THANK YOU, SCOTT. WE CAN NOW PROCEED TO CONSIDERATION OF CLIN2-17127. DR. LAM.
DR. LAM: THANK YOU. SO ON TO THE SECOND

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APPLICATION. THIS IS A GENE-MODIFIED STEM CELL THERAPY FOR ARTEMIS SCID, ART-SCID. AND THE GOAL OF THIS PROJECT IS TO COMPLETE A PHASE 2 TRIAL AND ALSO SUBMIT A BLA. AND THEY'RE REQUESTING JUST UNDER 15 MILLION WITH NO CO-FUNDING, AND THIS IS A CALIFORNIA ORGANIZATION.

SO BACKGROUND ON THIS DISEASE. SO IT IS ALSO A DIFFERENT VARIETY, I SUPPOSE, OF THE SCID. SO ESSENTIALLY NO FUNCTIONING IMMUNE SYSTEM. AND, AGAIN, THIS IS ALSO FATAL IF NOT TREATED. AND THIS PARTICULAR VARIATION OF THE SCID DISPROPORTIONATELY IMPACTS NATIVE AMERICAN POPULATIONS. AND THE CURRENT STANDARD OF CARE TRANSPLANT HAS MORE COMPLICATIONS IN ARTEMIS SCID COMPARED TO OTHER TYPES OF SCID. AND THEY OFTENTIMES NEED FREQUENT EXPENSIVE TREATMENTS, ONGOING TREATMENTS, BECAUSE THE IMMUNE SYSTEMS CANNOT BE FULLY RESTORED EVEN WITH A SUCCESSFUL TRANSPLANT.

SO THE PROPOSITION VALUE OF THE PROPOSED THERAPY IS TO MODIFY THE PATIENT'S OWN BLOOD STEM CELLS WITH A FUNCTIONAL COPY OF THE DEFECTIVE GENE AND WITH THE GOAL OF RESTORING A HEALTHY IMMUNE SYSTEM. AND, AGAIN, THE PATIENT'S OWN CELLS WILL REDUCE THE RISK OF TRANSPLANTATION SUCH AS THE GRAFT REJECTION. AND ALSO THE DATA TO DATE HAS SHOWN THAT

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THERE'S MORE COMPLETE RESTORATION OF THE IMMUNE SYSTEM WITH THIS METHOD.

AND THIS IS A CIRM PROJECT AS IT'S DERIVED FROM STEM CELLS AND IS A GENE THERAPY.

THE CIRM PORTFOLIO PROJECTS, SO THERE IS A PHASE 1 TRIAL THAT IS CLOSING FOR THE SAME PRODUCT AND PROJECT. AND THIS IS, AGAIN, A PHASE 2 TRIAL. SO A CONTINUATION.

THE APPLICANT TEAM HAS RECEIVED PRIOR CIRM FUNDING FOR SEVERAL STAGES ALONG THE DEVELOPMENT OF THE SAME PRODUCT AS YOU CAN SEE HERE. SO THEY'VE BEEN FUNDED FROM PRECLINICAL THROUGH IND-ENABLING AT THE PHASE 1 TRIAL.

SO FOR THE APPLICATION REVIEW SUBCOMMITTEE'S CONSIDERATION IS CLIN2-17127, GENE THERAPY FOR ARTEMIS DEFICIENT SEVERE COMBINED IMMUNODEFICIENCY USING A CELL INACTIVATING LENTIVIRAL VECTOR.

THE GRANTS WORKING GROUP RECOMMENDATION WAS A UNANIMOUS RECOMMENDATION TO FUND, AND THE DEI SCORE FOR THIS APPLICATION IS AN 8, AND THE CIRM TEAM CONCURS WITH THE GRANTS WORKING GROUP RECOMMENDATION TO FUND FOR THE AWARD AMOUNT OF JUST UNDER 15 MILLION. SO I'LL HAND IT BACK TO CHAIR IMBASCIANI.

CHAIRMAN IMBASCIANI: THANK YOU, HAYLEY. THANK YOU FOR THE RECOMMENDATION FROM THE REVIEW TEAM. I WOULD LIKE TO HAVE A MOTION TO OPEN UP DISCUSSION PLEASE.

DR. SOUTHARD: MARV SOUTHARD MOVES.

CHAIRMAN IMBASCIANI: YES. MARVIN, THAT WAS A MOTION TO FUND, YES?

DR. SOUTHARD: YES.

CHAIRMAN IMBASCIANI: OKAY. AND WE HAVE A SECOND?

MR. TOCHER: NOT AT THE MOMENT.

MR. FISCHER-COLBRIE: SECOND, MARK FISCHER-COLBRIE.

MR. TOCHER: THANK YOU, MARK.

CHAIRMAN IMBASCIANI: THANK YOU, MARK. OKAY. I'D LIKE TO OPEN THE FLOOR TO DISCUSSION FROM BOARD MEMBERS. I DON'T SEE ANY HANDS. OKAY. IS THERE ANY MEMBER OF THE PUBLIC THAT WOULD LIKE TO ADDRESS THIS APPLICATION?

MS. MANDAC: NO HANDS RAISED.

CHAIRMAN IMBASCIANI: AND THERE ARE NONE RAISED. OKAY. SCOTT, I KNOW YOU JUST DID, BUT YOU NEED TO DO IT AGAIN. ROLL CALL VOTE.

MR. TOCHER: ALL RIGHT. JUST ONE MOMENT. AND THIS IS A MOTION TO FUND CLIN2-17127.

CHAIRMAN IMBASCIANI: YES.
MR. TOCHER: JUDY CHOU. LEONDRA CLARK-HARVEY. ANNE-MARIE DULIEGE.
DR. DULIEGE: YES.
MR. TOCHER: MARK FISCHER-COLBRIE.
MR. FISCHER-COLBRIE: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: 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.
MR. TOCHER: MARV SOUTHARD. MARV, I THINK YOU MAY BE ON MUTE.
DR. SOUTHARD: I DON'T THINK SO. YES.
MR. TOCHER: OKAY. THANK YOU. MAYBE IT WAS JUST ME. KAROL WATSON.
DR. WATSON: YES.
MR. TOCHER: KEVIN XU.

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DR. XU: YES.

MR. TOCHER: IT'S LIKE WE'RE ON A RADIO PROGRAM. GREAT. THAT MOTION CARRIES. THANKS VERY MUCH. I THINK I HAVE EVERYONE'S VOTE RECORDED. AND, VITO, THE MOTION CARRIES.

CHAIRMAN IMBASCIANI: THANK YOU VERY MUCH. OKAY. SO WE'RE COMING NOW TO THE PART OF THE MEETING FOR PUBLIC COMMENT. AND I WOULD LIKE TO ASK GIL -- I SEE WE HAVE A MEMBER OF THE PUBLIC IN ATTENDANCE WHO WOULD LIKE TO MAKE A COMMENT. I'D ASK THE GENTLEMAN PLEASE STATE YOUR NAME, AND YOU HAVE THREE MINUTES TO ADDRESS THE BOARD.

MS. MANDAC: DR. RAMKUMAR, I DON'T KNOW IF YOU CAN HEAR US.

CHAIRMAN IMBASCIANI: DR. RAMKUMAR, CAN YOU HEAR ME?

DR. RAMKUMAR: CAN YOU HEAR ME?

MS. MANDAC: YES. TURN OFF THE YOUTUBE, DR. RAMKUMAR.

CHAIRMAN IMBASCIANI: DR. RAMKUMAR, CAN YOU HEAR ME?

DR. RAMKUMAR: I CAN HEAR YOU, BUT I KEEP HEARING AN ECHO.

MS. MANDAC: IF YOU HAVE IT OPEN ON YOUTUBE, COULD YOU PLEASE TURN OFF THE BROWSER?

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SORRY. WE CAN'T -- DR. RAMKUMAR, WE CAN SEE YOUR LIPS MOVING, BUT UNFORTUNATELY THERE'S NO AUDIO.

DR. RAMKUMAR: HOW ABOUT NOW?

CHAIRMAN IMBASCIANI: YES.

MS. MANDAC: YES.

CHAIRMAN IMBASCIANI: GREAT.

DR. RAMKUMAR: OKAY. SORRY FOR THE TECHNICAL ISSUES.

CHAIRMAN IMBASCIANI: THAT'S OKAY. THE CLOCK HAS NOT STARTED YET. GO AHEAD.

DR. RAMKUMAR: OKAY, GREAT. HI. MY NAME IS RAM. I'M THE COO FOR OCULOGENEX. AND WE ARE DEVELOPING A PROMISING GENE THERAPY FOR AN UNMET NEED IN THE OCULAR SPACE THAT WILL BENEFIT OVER TWO MILLION CALIFORNIANS WITH AMD. A PRE-IND MEETING PAVED A REALLY CLEAR PATH FOR US TO GET TO FIRST-IN-HUMAN TRIALS WITH STRONG FDA SUPPORT OF OUR PLANS.

WE SUBMITTED A CLIN1 GRANT PROPOSAL IN JULY AND WERE NOTIFIED IN OCTOBER THAT WE WILL NOT PROCEED TO THE GWG MERIT REVIEW PRIOR TO MAKING OUR FUNDING DECISIONS. AND WE DIDN'T RECEIVE ANY DETAILS AT THAT TIME. I DID ATTEND THE JUNE ARS MEETING WHERE DR. SAMBRANO PRESENTED THE NEW QUALIFYING PROCESS THAT WAS APPROVED BY THE ICOC.

AND I DID LISTEN IN TO THE DETAILS OF THE QUALIFYING PROCESS THAT BROUGHT AN OBJECTIVE ELEMENT AND A SUBJECTIVE ELEMENT. AND WHEN I COORDINATED OUR INPUT WITH CIRM, I DID GET A REPLY YESTERDAY THAT KIND OF SAID THAT DURING THE QUALIFYING PROCESS, WE RECEIVED A SCORE OF 3 OUT OF 6 ON THE OBJECTIVE PORTION AND 13 OUT OF 20 ON THE SUBJECTIVE PORTION. AND DR. LAM WAS KIND ENOUGH TO ATTACH THE TWO GWG REVIEWER COMMENTS ALONG WITH THE SCORES.

WHEN WE REVIEWED THAT, I REALIZED THAT THIS PROCESS DID NOT WORK TO OUR ADVANTAGE PRIMARILY BECAUSE I BELIEVE AS A NONPIPELINE PROPOSAL WE ARE DISADVANTAGED FROM THE FIRST ELEMENT OF THE PROCESS, THE OBJECTIVE PORTION. AND UNDER THE SUBJECTIVE PORTION, OF THE TWO REVIEWERS, IT WAS OBVIOUS TO US THAT ONE REVIEWER EITHER DID NOT HAVE THE BACKGROUND TO EVALUATE THE PROPOSAL OR MADE COMMENTS AGAINST THE SCORE THAT WERE WRONG IN THREE OF THE FOUR CATEGORIES. SO YOU GET A SCORE OF FIVE FOR EACH OF FOUR CRITERIA IN THE SECOND CATEGORY THAT'S CALLED SUBJECTIVE. AND WE FOUND THAT THREE OUT OF THE FOUR WERE BASED ON ASSUMPTIONS THAT WERE ALL WRONG.

SO WE SAID WE NEEDED TO BRING THIS TO YOUR ATTENTION AND SEE HOW WE COULD, AS A CALIFORNIA CORPORATION WITH A PROMISING THERAPY IN OUR HANDS,

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GET SUPPORT FROM CIRM AND WORK THROUGH THIS PROCESS. I UNDERSTAND IT'S --

MS. MANDAC: THANK YOU SO MUCH, DR. RAMKUMAR.

CHAIRMAN IMBASCIANI: THANK YOU, DR. RAMKUMAR. DOES THAT REQUIRE A RESPONSE? I DON'T THINK SO. THANK YOU FOR YOUR REMARKS. THEY'RE DULY NOTED.

ANY OTHER MEMBER OF THE PUBLIC WISH TO ADDRESS THE BOARD ON THE APPLICATIONS THAT HAVE BEEN SUBMITTED OR ON ANY OTHER ITEM NOT ON THE AGENDA? NO. OKAY.

FOLKS, I THINK WE'VE COME TO THE END OF THE AGENDA THEN. THANK YOU VERY MUCH FOR YOUR PARTICIPATION. ANY FINAL COMMENTS FROM ANYONE? IF NOT, WE ARE ADJOURNED.

MR. TOCHER: THANKS, EVERYONE, FOR MAKING IT TO THE MEETING.

(THE MEETING WAS THEN CONCLUDED AT 9:30 A.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 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 21, 2024, 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
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