BEFORE THE

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

REGULAR MEETING

LOCATION: AS INDICATED ON THE AGENDA

DATE: JULY 24, 2019
11 A.M.

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

FILE NO.: 2019-14

I N D E X

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JULY 24, 2019; 11:00 A.M.

CHAIRMAN THOMAS: GOOD MORNING, EVERYBODY, AND WELCOME TO THE REGULAR MEETING OF THE ICOC AND APPLICATION REVIEW SUBCOMMITTEE FOR JULY 2019. WE HAVE QUITE A CROWD IN THE OFFICE HERE UP IN OAKLAND. I'M NOT SURE IF THERE ARE OTHERS AT OUR DIFFERENT SITES; BUT WITHOUT FURTHER ADO, LET'S GET GOING. MARIA, WILL YOU PLEASE CALL THE ROLL.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES, I'M HERE.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: HERE.

MS. BONNEVILLE: SHERRY LANSING.

MS. LANSING: YES, I'M HERE.

MS. BONNEVILLE: DAVE MARTIN.

DR. MARTIN: HERE.

MS. BONNEVILLE: LAUREN MILLER. ADRIANA PADILLA.

DR. PADILLA: YES, HERE.

MS. BONNEVILLE: JOE PANETTA.

MR. PANETTA: HERE.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. BONNEVILLE: ROBERT QUINT. 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 OTHER BOARD MEMBERS WHOSE NAME I DID NOT CALL WHO ARE ON THE PHONE?

DR. FINE: YES. LEON FINE.

MS. BONNEVILLE: THANK YOU.

DR. SANDMEYER: SUZANNE SANDMEYER.

MS. BONNEVILLE: THANK YOU.

DR. GASSON: JUDY GASSON.

MS. BONNEVILLE: THANK YOU, JUDY.

THANK YOU VERY MUCH. WE HAVE A QUORUM.

CHAIRMAN THOMAS: THANK YOU, MARIA.

ON TO ITEM NO. 3, CONSIDERATION OF APPLICATIONS SUBMITTED IN RESPONSE TO CLINICAL TRIAL STAGE PROJECTS, CLIN1, 2, AND 3. TURN THE MEETING OVER AT THIS POINT TO MR. SHEEHY.

MR. SHEEHY: OKAY. SO DR. PATEL IS GOING TO TAKE US THROUGH THE RECOMMENDATION FOR THE ONE APPLICATION WE HAVE.

DR. PATEL: THANK YOU, MR. SHEEHY. I HAVE THE EASY TASK TODAY OF THE CLINICAL APPLICATIONS. SO I'M GOING TO DO THE PRESENTATION AND THEN TURN IT BACK OVER TO YOU.

SO, AS YOU ALL KNOW, THE CLINICAL PROGRAM IS COMPOSED OF THREE DISTINCT FUNDING OPPORTUNITIES RANGING FROM IND-ENABLING PRECLINICAL PROJECTS TO PHASE 1, 2, AND 3 CLINICAL TRIALS. THE SINGLE APPLICATION UP FOR YOUR REVIEW TODAY IS A CLIN2 APPLICATION FOR A PHASE 1 CLINICAL TRIAL.

JUST A REMINDER ON THE WAY THAT OUR GRANTS WORKING GROUP SCORES THESE APPLICATIONS. THEY GIVE IT A SCORE OF 1, 2, OR 3. IF THE APPLICATION HAS EXCEPTIONAL MERIT AND WARRANTS FUNDING, IT GETS A SCORE OF 1. IF IT NEEDS IMPROVEMENT AND DOES NOT WARRANT FUNDING BUT CAN BE RESUBMITTED, IT GETS A SCORE OF 2. AND, LASTLY, IF IT'S SUFFICIENTLY FLAWED THAT IT DOES NOT WARRANT FUNDING AND SHOULD

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NOT BE RESUBMITTED FOR SIX MONTHS, IT GETS A SCORE OF 3. AND I'LL HIGHLIGHT THE GWG SCORES AT THE END OF THE PRESENTATION.

TO GIVE YOU AN UPDATE ON THE CLINICAL BUDGET. THIS IS FOR THE BIG BUCKET, THE GENERAL CLINICAL PROGRAM DESIGNED NOT FOR THE SICKLE CELL PROGRAM. THE ANNUAL ALLOCATION FOR THIS WAS $93 MILLION FOR 2019. TO DATE THE BOARD HAS APPROVED $60 MILLION IN FUNDING FOR CLIN AWARDS. THE CURRENT APPLICATION UP FOR REVIEW TODAY IS $9.3 MILLION AS REQUESTED. IF YOU WERE TO APPROVE THAT FOR FUNDING, THAT WOULD REMAIN -- THAT WOULD HAVE AN UNUSED BALANCE OF $23.7 MILLION GOING FORWARD FOR THE PROGRAM FOR THE REST OF THE YEAR.

SO, AS YOU KNOW, THE CIRM TEAM SETS INTERNAL TARGETS BASED ON THE ANNUAL ALLOCATION; AND FOR THE CLIN PROGRAM, WE SET A TARGET OF EIGHT TRIALS FOR CLIN2 AWARDS AND TWO CLIN1 AWARDS. WE'VE MET THE CLIN1 TARGET. AGAIN, IT DOES NOT MEAN THAT YOU CANNOT FUND ADDITIONAL ONES. FOR CLIN2, WE'VE FUNDED SIX TRIALS TO DATE. AND IF YOU APPROVE TODAY'S, THAT WOULD MAKE IT SEVEN OUT OF EIGHT FOR THE TARGET.

SO TO GET TO THE CURRENT APPLICATION UP FOR REVIEW TODAY, THIS IS CLIN2-11574, AND THE

THERAPY IS AUTOLOGOUS HER2 TARGETED CAR-T CELLS, AND THE T-CELLS HERE ARE WITH A STARTING POPULATION OF 90 STEM MEMORY T-CELLS. THE INDICATION IS HER2 POSITIVE BREAST CANCER THAT HAS METASTASIZED TO THE CENTRAL NERVOUS SYSTEM, AND IT'S A PHASE 1 TRIAL. THEY'RE REQUESTING $9.29 MILLION, AND THE MAXIMUM ALLOWABLE FOR THIS CATEGORY IS $12 MILLION, AND THEY'RE NOT REQUIRED TO HAVE CO-FUNDING AT THIS STAGE.

SO TO GIVE YOU A BRIEF BACKGROUND ON THE CLINICAL SIDE AS WELL AS THE VALUE PROPOSITION FOR THIS PARTICULAR THERAPY, AS YOU ALL KNOW, BREAST CANCER IS THE MOST COMMON CANCER IN WOMEN. HER2 POSITIVE CANCER REPRESENTS ABOUT 20 TO 25 PERCENT OF THE TOTAL BREAST CANCER POPULATION, AND IT'S HIGHLY METASTATIC. AND IT'S ESTIMATED THAT UP TO 50 PERCENT OF THESE PATIENTS CAN DEVELOP CNS TUMORS. IF I'VE DONE MY MATH CORRECTLY, THAT MEANS THAT THE TARGET PATIENT POPULATION FOR THIS PARTICULAR THERAPY WILL BE ABOUT 10 PERCENT OF THE TOTAL BREAST CANCER POPULATION.

SO WHILE THESE METASTASES ARE TREATED WITH A COMBINATION OF SURGERY, RADIATION, CHEMOTHERAPY, AND IMMUNOTHERAPY, THE PROGNOSIS AND QUALITY OF LIFE FOR THESE PATIENTS REMAINS VERY POOR. AND PART OF

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THE REASON FOR THAT IS THAT HER2 TARGETED IMMUNOTHERAPY, WHICH HAS BEEN EFFECTIVE IN BREAST CANCER, IS ONLY EFFECTIVE FOR EXTRACRANIAL METASTASES, AND IT HAS LIMITED PENETRATION INTO THE BRAIN DUE TO NOT BEING ABLE TO CROSS THE BLOOD-BRAIN BARRIER. SO THE VALUE PROPOSITION FOR THIS PARTICULAR APPROACH IS THAT YOU CAN HAVE HER2 TARGETED IMMUNOCELLULAR THERAPY DELIVERED LOCALLY AND HAVE A SUSTAINED ANTITUMOR RESPONSE IN THE CNS FOR BOTH BRAIN AS WELL AS LEFT LOBE MEDIAL TUMORS.

IF IT'S SHOWN TO BE EFFECTIVE, IT HAS THE POTENTIAL TO GREATLY IMPROVE SURVIVAL AND QUALITY OF LIFE FOR THESE PATIENTS.

THE REASON THAT WE ARE REVIEWING THIS PARTICULAR APPLICATION IS BECAUSE THE CELL THERAPY INCLUDES GENE-MODIFIED NAIVE AND STEM MEMORY T-CELLS, WHICH MEETS THE PROGENITOR CELL DEFINITION IN PROP 71.

I WANT TO HIGHLIGHT THAT THERE IS A RELATED CIRM PROJECT IN OUR PORTFOLIO CURRENTLY. THIS IS A CLIN2 AWARD FOR A PHASE 1 TRIAL FOR IL-13 RECEPTOR CAR-T CELLS FOR MALIGNANT GLIOMA. AGAIN, THE INDICATION THERE IS DIFFERENT, BUT BOTH OF THESE PROJECTS, THE ONE CURRENTLY UNDER REVIEW FOR HER2 AS WELL AS THE PREVIOUSLY FUNDED IL-13 CAR-T THERAPY

BEING CO-DEVELOPED. AND, THUS, THERE'S SIMILAR CAR-T TECHNOLOGY AT PLAY AS WELL AS SIMILAR DELIVERY MECHANISMS. AND THE TRIALS INFORM EACH OTHER AS WELL.

BOTH OF THESE TRIALS ACTUALLY STEM FROM A DISCOVERY STAGE PROJECT FUNDED BY CIRM WHERE THEY WERE DISCOVERED AND SHOWN TO HAVE EFFICACY IN PRECLINICAL MODELS. THIS PARTICULAR AWARD WAS STARTED IN 2013 AND ENDED IN 2016. THE AWARD AMOUNT FOR THAT WAS 5.22 MILLION, AND THEY ACHIEVED ALL FOUR OF THEIR MILESTONES EITHER ON TIME OR WITH MINOR DELAYS.

AS PROMISED, THIS IS A BREAKDOWN OF THE GRANTS WORKING GROUP REVIEW SCORES. FIFTEEN MEMBERS SCORED THE APPLICATION. ELEVEN GAVE IT A SCORE OF 1 AND FOUR GAVE IT A SCORE OF 2, MAKING IT A TIER I RECOMMENDATION FROM THE GRANTS WORKING GROUP. THE CIRM TEAM CONCURS WITH THAT RECOMMENDATION TO FUND THE APPLICATION FOR THE AWARD AMOUNT REQUESTED WHICH IS ROUGHLY $9.29 MILLION.

MR. SHEEHY.

MR. SHEEHY: SURE. SO DO I HAVE A MOTION TO ACCEPT THE CIRM TEAM RECOMMENDATION?

DR. DULIEGE: AYE. THIS IS ANNE-MARIE.

MR. SHEEHY: DO I HAVE A SECOND?

MR. PANETTA: THIS IS JOE. YES.

MR. SHEEHY: SECOND FROM JOE PANETTA. DO WE HAVE ANY BOARD DISCUSSION ON THIS?

DR. DULIEGE: TWO QUICK QUESTIONS IF THAT'S OKAY.

MR. SHEEHY: SURE.

DR. DULIEGE: SO ONE IS HOW ARE THE CAR-T CELLS DELIVERED INTO THE CNS? AND MY SECOND QUESTION IS IS THE COST OF $9.2 MILLION REPRESENTING, IN FACT, THE ENTIRE COST OF THIS PHASE 1 TRIAL, AND WHAT'S THE SIZE OF THE PHASE 1 TRIAL, NUMBER OF PATIENTS EXPECTED TO BE ENROLLED, AND HAS IT ACTUALLY STARTED?

DR. PATEL: THANK YOU, MR. SHEEHY. SO THE FIRST QUESTION WITH RESPECT TO THE DELIVERY MECHANISM, THIS IS REGIONALLY DELIVERED INTRAVENTRICULARLY. SO THEY USE A RESERVOIR SYSTEM TO DELIVER THE CELLS.

WITH RESPECT TO THE SECOND QUESTION IN TERMS OF THE PATIENTS, SO THERE WAS AN INITIAL COHORT THAT WAS TREATED WITH A DIFFERENT CELL POPULATION. FOR THE PARTICULAR TRIAL THEY'RE ASKING US FOR, I BELIEVE THE TOTAL NUMBER OF PATIENTS TO BE TREATED IS 21.

DR. DULIEGE: AND I ASSUME WE DON'T HAVE

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ANY RESULTS FROM THE INITIAL COHORT?

DR. PATEL: SO FROM THE INITIAL COHORT, WHICH WAS A DIFFERENT CELL POPULATION, THE RESULTS WERE PRESENTED TO THE GRANTS WORKING GROUP, AND THEY FOUND THE RESULTS TO BE ENCOURAGING ENOUGH TO SUPPORT THIS PARTICULAR TRIAL.

DR. DULIEGE: OKAY. GREAT. THANK YOU VERY MUCH.

MR. PANETTA: I JUST HAVE TWO BRIEF QUESTIONS JUST TO FOLLOW UP ON ANNE-MARIE'S QUESTION. SO OBVIOUSLY THE INITIAL TRIAL THAT WAS DONE AND THIS ONE ARE BASICALLY SAFETY TRIALS. SO OBVIOUSLY WE WON'T SEE ANY EFFICACY OUT OF THESE TRIALS. I GUESS THAT'S NOT REALLY A QUESTION. BUT THIS SEEMS LIKE AN EXCEPTIONAL PROPOSAL, AND I'M CURIOUS IF IT'S POSSIBLE TO LEARN WHY THERE WERE FOUR VOTES THAT GAVE IT A SCORE OF TWO.

DR. PATEL: I CAN COMMENT ON THAT. WITH RESPECT TO THE FOUR REVIEWERS WHO GAVE IT A SCORE OF 2, THERE WAS A MIX OF REASONS FOR THAT. ONE OF THE REASONS WAS THAT THEY FELT THAT -- SOME OF THEM FELT THAT, BECAUSE THERE IS THIS ONGOING TRIAL IN GLIOBLASTOMA WITH THE IL-13 RECEPTOR CAR-T CELLS, GETTING MORE DATA FROM THAT TRIAL WOULD BETTER INFORM THE EXECUTION OF THE CURRENT TRIAL. AGAIN,

THEY'RE DIFFERENT INDICATIONS, AND THAT OTHER TRIAL IS STUDYING DIFFERENT CELL POPULATIONS AS WELL AS DIFFERENT DELIVERY MECHANISMS.

MR. PANETTA: OKAY. SO BASICALLY NOT A CRITICISM OF THIS TRIAL, BUT YOU GET MORE INFORMATION FROM THE OTHER TRIAL FIRST?

DR. PATEL: CORRECT.

MR. PANETTA: OKAY. THANKS.

DR. MARTIN: I HAVE A QUESTION ABOUT THE CONSTRUCT OF THE CAR. JUST VERY BRIEFLY, THIS IS, PRESUMABLY, AN SCFV HER2 CONSTRUCT FOR THE TARGETING DOMAIN. AND WHAT IS THE INTRACELLULAR CONSTRUCT, AND IS IT ONE THAT IS WIDELY USED OR SOMETHING NOVEL? IS IT A CD 28, A 41-BB? JUST TELL US SOMETHING ABOUT WHY -- ABOUT THE CAR. WHAT ARE THE EXPECTATIONS? WHAT SHOULD BE THE EXPECTATIONS OF ITS EFFICACY? IS IT NOVEL, OR IS IT TRADITIONAL?

DR. PATEL: WE WANT TO PROTECT THE CONFIDENTIALITY OF THE APPLICANT, AND WE ARE NOT ABLE TO REVEAL THAT WITHOUT GOING TO CLOSED SESSION.

DR. MARTIN: THAT SHOULDN'T BE CONFIDENTIAL. IS IT -- ALL RIGHT. I WON'T PURSUE IT.

DR. PATEL: IT IS -- FIRST OF ALL, I JUST CHECKED THE SUMMARY, AND IN THERE IT'S A BB, SO

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YOU'RE RIGHT, THAT IT'S GOING TO BE ONE OF THE KNOWN ONES.

DR. MARTIN: THANK YOU.

MR. SHEEHY: ARE THERE ADDITIONAL QUESTIONS? COMMENTS? ANY PUBLIC COMMENT ABOUT THIS APPLICATION?

DR. PRICEMAN: MEMBERS OF THE BOARD, MEMBERS OF CIRM, GOOD MORNING. I'M SAUL PRICEMAN. I'M THE PRINCIPAL INVESTIGATOR OF THIS CLIN2 APPLICATION. THANK YOU FOR THE OPPORTUNITY TO SPEAK TODAY.

ONE OF THE GREAT SUCCESS STORIES IN CANCER TREATMENT IS TARGETING THE HER2 ONCOGENE FOR BREAST CANCER. IT'S LANDED IN REMARKABLE FDA-APPROVED THERAPIES, EXTENDING THE LIVES OF PATIENTS WITH THIS DISEASE. UNFORTUNATELY, AS MANY AS 50 PERCENT OF HER2 POSITIVE BREAST CANCER PATIENTS ULTIMATELY DEVELOP BRAIN METASTATIC DISEASE FOR WHICH THERE IS ABSOLUTELY NO EFFECTIVE THERAPY.

WE PLAN TO BREAK THAT BARRIER WITH OUR HER2 TARGETED CAR-T CELL THERAPY. CIRM HAS DONE A TREMENDOUS JOB OF FUNDING THE DEVELOPMENT OF THERAPIES FOR MULTIPLE TYPES OF CANCER. SURPRISINGLY, THERE ARE NO FUNDED PROJECTS SPECIFICALLY FOCUSED ON BREAST CANCER OR BRAIN

METASTATIC DISEASE.

WE HOPE YOU WILL ELIMINATE THIS GAP TODAY BECAUSE WE BELIEVE OUR UNIQUE CAR-T CELL APPROACH WILL ULTIMATELY PRODUCE LIFE-EXTENDING THERAPY FOR THESE PATIENTS.

THE PHASE 1 CLINICAL TRIAL WE PROPOSE WAS HIGHLY RECOMMENDED BY THE GWG REVIEWERS WHO WERE SUPPORTIVE OF OUR RATIONALE, OUR TEAM, AS WELL AS OUR CLINICAL DATA TO DATE, AND ACKNOWLEDGED THE POTENTIAL BREAKTHROUGH STATUS OF THIS TRIAL.

FOR THE PAST 20 YEARS, CITY OF HOPE HAS FOCUSED INTENSELY ON DEVELOPING CAR-T CELL APPROACHES FOR TREATING THE MOST INTRACTABLE SOLID TUMORS. IN THE EARLY 2000S, WE WERE THE FIRST TO DEMONSTRATE SOLID TUMOR CAR-T CELL THERAPY TREATMENT IN PATIENTS. AND RECENTLY WE WERE THE FIRST TO REPORT OUR REMARKABLE RESPONSE FOR PATIENTS WITH GLIOBLASTOMA. WE HAVE GAINED CRUCIAL INFORMATION FROM THOSE EARLY TRIALS REGARDING BOTH THE FEASIBILITY AND SAFETY OF OUR INTRAVENTRICULAR ROUTE OF DELIVERY AS WELL AS THE MANUFACTURING PROCESS FOR STEM MEMORY CAR-T CELL THERAPY. SINCE NO THERAPIES TO DATE HAVE BEEN EFFECTIVE FOR THESE PATIENTS WITH HER2 POSITIVE BRAIN METASTATIC DISEASE, WE ARE ANXIOUS TO MOVE QUICKLY FORWARD WITH THE PHASE 1

TRIAL.

FOR THE PATIENTS WITH THIS DISEASE, AN EFFECTIVE THERAPY IS DESPERATELY NEEDED. WE'D LIKE TO THANK THE REVIEWERS, ICOC, AND CIRM FOR FINDING MERIT IN OUR APPLICATION. WE HOPE YOU WILL FUND THIS IMPORTANT EARLY PHASE CLINICAL TRIAL. THANK YOU.

MR. SHEEHY: THANK YOU. IS THERE ANY OTHER -- SENATOR TORRES.

MR. TORRES: YES. I WAS A PATIENT ADVOCATE REVIEWER ON YOUR GRANT. AND AS THE SON OF A BREAST CANCER PATIENT WHO HAD A SIMILAR DIAGNOSIS, SHE FIRST RECOVERED FROM BREAST CANCER IN 1994, SO I PUT HER IN THE FIRST TAMOXIFEN TRIAL, AND IN 2012 WE LOST HER, BUT SHE HAD A GOOD LIFE.

WITH THAT PERSONAL EXPERIENCE AND ALSO KNOWING OTHERS THAT HAVE BEEN IN THAT HORRIBLE SITUATION WHERE THERE'S NOTHING AVAILABLE ONCE THE GLIOMA BEGINS, THIS IS A PERFECT OPPORTUNITY FOR US TO GET AHEAD OF THE ISSUE HERE. THAT'S WHY I SUPPORT IT.

DR. PRICEMAN: THANK YOU.

MR. SHEEHY: THANK YOU, SENATOR TORRES. ANY OTHER COMMENTS EITHER FROM THE PUBLIC OR FROM THE BOARD?

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DR. MARTIN: I HAVE ANOTHER QUESTION. IN THE CLINICALTRIALS.GOV OF CAR-T STUDIES, OF WHICH THERE ARE ABOUT 300, ARE ANY OF THEM HER2 SCFV CAR-TS THAT ARE FOCUSED IN THE SAME -- FOR THE SAME INDICATION?

DR. PRICEMAN: THERE ARE, TO OUR KNOWLEDGE, TWO ONGOING TRIALS FOR HER2 TARGETED CAR-T CELLS, ONE SYSTEMIC DELIVERY FOR GLIOBLASTOMA, THE OTHER SYSTEMIC DELIVERY FOR SARCOMA. TO OUR KNOWLEDGE, THIS IS THE FIRST HER2 CAR-T TRIAL FOR BRAIN METASTATIC DISEASE.

DR. MARTIN: THANK YOU.

MR. SHEEHY: OTHER COMMENTS OR QUESTIONS FROM THE PUBLIC OR FROM THE BOARD? COULD YOU CALL THE ROLL, MS. BONNEVILLE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

MS. BONNEVILLE: SHERRY LANSING.

MS. LANSING: YES.

MS. BONNEVILLE: DAVE MARTIN.

DR. MARTIN: YES.

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MS. BONNEVILLE: ADRIANA PADILLA.
DR. PADILLA: YES.
MS. BONNEVILLE: JOE PANETTA.
MR. PANETTA: YES.
MS. BONNEVILLE: FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: YES.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
MS. BONNEVILLE: THE MOTION CARRIES.
MR. SHEEHY: THANK YOU.
OKAY. I THINK WE'RE TO THE NEXT AGENDA ITEM, WHICH IS CONSIDERATION OF THE TRANS APPLICATIONS. THANK YOU, DR. PRICEMAN. GOOD LUCK

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WITH YOUR AWARD.

THE REPORTER: MR. CHAIRMAN, THIS IS BETH. I HEAR A LOT OF PAPER RATTLING. IF WE COULD ASK MEMBERS TO PLEASE MUTE THEIR PHONES IF THEY'RE NOT SPEAKING.

MR. SHEEHY: SURE.

THE REPORTER: THANK YOU VERY MUCH.

MR. SHEEHY: I HOPE EVERYONE HEARD BETH, WHO, GOD BLESS HER, I THINK, HAS BEEN WITH US SINCE THE BEGINNING AND HAS DONE AN EXTRAORDINARY JOB.

THE REPORTER: THANK YOU FOR THAT.

MR. SHEEHY: NO ONE CAN SAY WE HAVEN'T BEEN TRANSPARENT. EVERY WORD SPOKEN IS RECORDED FAITHFULLY BY BETH GOING BACK NOW WELL OVER A DECADE.

SO WHO'S GOING TO TAKE US, DR. SAMBRANO --

DR. SAMBRANO: YES.

MR. SHEEHY: -- THROUGH THE TRANS?

DR. SAMBRANO: THANK YOU, MR. SHEEHY. SO GOOD MORNING, EVERYONE. I'LL TAKE YOU THROUGH THE PRESENTATION AND OVERVIEW OF THE GRANTS WORKING GROUP RECOMMENDATIONS FOR THIS CYCLE FOR THE TRANSLATIONAL PROGRAMS.

AND SO JUST A QUICK REMINDER OF WHERE IT FITS AMONG OUR FUNDING OPPORTUNITIES, THE

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TRANSLATIONAL PROGRAM TAKES SINGLE PRODUCT CANDIDATES, WHETHER OR NOT THROUGH OUR OWN DISCOVERY PROGRAM, AND TAKES THEM TO THE POINT WHERE THEY CAN BEGIN OR INITIATE IND-ENABLING ACTIVITIES AND ON INTO THE CLINIC. AND AS SUCH, THE OBJECTIVE IS TO TAKE PROMISING STEM CELL-BASED PROJECTS THAT WILL ACCELERATE THE COMPLETION OF THOSE TRANSLATIONAL STAGE ACTIVITIES AND ADVANCE THEM ULTIMATELY TO THE CLINIC.

AND TYPICALLY WHAT QUALIFIES FOR THE TRAN PROGRAM ARE FOUR DIFFERENT PRODUCT TYPES: THERAPEUTICS, DIAGNOSTICS, MEDICAL DEVICES, AND TOOLS. FOR THE ONLY CYCLE THAT WE HAVE HAD IN 2019, AS WAS INDICATED PREVIOUSLY, THIS WAS GOING TO BE LIMITED ONLY TO THERAPEUTIC CANDIDATES, SO ONLY THOSE QUALIFIED FOR THIS PARTICULAR CYCLE.

SO FOR THERAPEUTICS, WHAT WE EXPECT IN TERMS OF APPLICANTS COMING IN IS THAT THEY HAVE A SINGLE CANDIDATE WHERE THEY HAVE DEMONSTRATED DISEASE-MODIFYING ACTIVITY IN AN APPROPRIATE MODEL. THE PROJECT OR THE AWARD WOULD TAKE THEM THROUGH THE KEY TRANSLATIONAL ACTIVITIES THAT, HOPEFULLY BY THE END OF THE AWARD, WILL ALLOW THEM TO COMPLETE A PRE-IND MEETING WITH THE FDA AND MOVE ON FROM THERE.

THE GRANTS WORKING GROUP LOOKS AT THESE

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APPLICATIONS WITH A FOCUS ON THESE FOUR KEY QUESTIONS IN TERMS OF EVALUATING THE MERIT OF THE APPLICATIONS.

FIRST, DOES THE PROJECT HOLD THE NECESSARY SIGNIFICANCE AND POTENTIAL FOR IMPACT? DOES IT HAVE A SOUND RATIONALE? IS THE PROJECT WELL-PLANNED AND DESIGNED? AND IS THE PROJECT FEASIBLE?

THE SCORING SYSTEM THAT THE GRANTS WORKING GROUP USES FOR THESE APPLICATIONS IS DIFFERENT FROM THE CLIN PROGRAM. HERE WE HAVE A SCALE OF ONE TO A HUNDRED. SO REVIEWERS THAT ARE SCORING APPLICATIONS BETWEEN 85 AND A HUNDRED MEANS THAT THEY'RE RECOMMENDING FUNDING IF FUNDS ARE AVAILABLE. IF THEY SCORE BETWEEN 1 AND 84, THEIR RECOMMENDATION IS TO NOT FUND. ALL APPLICATIONS ARE SCORED BY THE SCIENTIFIC MEMBERS THAT HAVE NO CONFLICTS. AND WHAT WE DO IS TAKE THE MEDIAN OF ALL INDIVIDUAL GWG SCORES TO DETERMINE WHAT THE FINAL SCORE IS.

SO IN THIS PARTICULAR CYCLE, WE HAD 19 APPLICATIONS THAT CAME THROUGH. SEVEN OF THEM WERE RECOMMENDED BY THE GRANTS WORKING GROUP. THE TOTAL APPLICANT REQUEST WITH THOSE SEVEN APPLICATIONS IS 30.7 MILLION. HOWEVER, THE FUNDS THAT ARE AVAILABLE, AT LEAST THAT WERE ALLOCATED TO THE TRANSLATIONAL PROGRAM FOR 2019, IS $20 MILLION. SO

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WE HAVE MORE RECOMMENDED THAN THE BUDGET WILL ALLOW.

AND SO AS SUCH, GIVEN THAT WE HAVE SEVEN MERITORIOUS APPLICATIONS, WE ARE MAKING A RECOMMENDATION TO YOU ABOUT HOW TO POTENTIALLY GO ABOUT THIS. SO --

MR. SHEEHY: ISN'T THAT PROGRAMMATIC REVIEW FOR THE BOARD?

DR. SAMBRANO: WELL, THE RECOMMENDATION IS OURS. THE PROGRAMMATIC REVIEW IS UP TO YOU. YOU CAN IGNORE OUR RECOMMENDATION.

MR. SHEEHY: THIS IS KIND OF NEW TO ME. I'M TRYING TO UNDERSTAND THE PROCESS.

DR. SAMBRANO: SURE.

MR. SHEEHY: IT'S CHANGED.

DR. SAMBRANO: SO THE PROCESS HASN'T CHANGED. OUR RECOMMENDATION IS DIFFERENT FROM WHAT WE HAVE HAD IN THE PAST. AND SO, GIVEN THE CIRCUMSTANCES, WE ARE PROVIDING A RECOMMENDATION, WHICH IS UP TO YOU IF YOU WANT TO ACCEPT IT OR NOT. WE CAN GO THROUGH OUR RATIONALE FOR IT.

MR. SHEEHY: IT'S VERY CONFUSING TO ME.

MR. TORRES: WE HAVE HAD RECOMMENDATIONS FROM THE STAFF BEFORE. CIRM RECOMMENDS BLAH AND THEN WE DECIDE.

MR. SHEEHY: USUALLY PROGRAMMATIC REVIEW

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HAS BEEN CONDUCTED BY THE BOARD.

DR. SAMBRANO: SHALL I PROCEED? OKAY.

SO OUR RECOMMENDATION IS IN TWO PHASES. SO THE FIRST IS WE HAVE $20 MILLION WHICH CAN COVER ABOUT FOUR APPLICATIONS. SO THOSE CAN BE ANY OF THE APPLICATIONS. BUT IN ADDITION, WE ARE SUGGESTING THAT THE REMAINING THREE OR THOSE THAT CANNOT BE FUNDED BE LEFT OPEN AS OPPOSED TO CLOSING THEM OUT. THERE ARE RECOVERED FUNDS THAT WE ARE LIKELY TO HAVE. CURRENTLY WE HAVE 19.1 MILLION WHICH WE WILL BRING TO THE FULL BOARD IN SEPTEMBER FOR ALLOCATION. THIS IS ONE WAY THAT THEY CAN BE ALLOCATED TO HELP COVER THOSE THAT THE 20 MILLION TODAY CAN'T COVER.

AND SO THAT'S THE FIRST PART. AND THE SECOND IS, BASED ON THE RANK ORDER, WE HAVE A SUGGESTION FOR HOW THAT APPROVAL MAY HAPPEN SO THAT THE BOARD COULD APPROVE THE TOP TWO SCORING APPLICATIONS, SELECT TWO AMONG THE THREE THAT ARE IN THE MIDDLE THAT ARE ALL IN THE NEUROLOGICAL FIELD. AND THEN WHATEVER REMAINS, THE LAST TWO AND ONE OF THE NEUROLOGICAL ONES, THAT THOSE REMAIN OPEN FOR CONSIDERATION IN SEPTEMBER AND AT THAT TIME, IF FUNDS ARE ALLOCATED, WHETHER OR NOT THEY SHOULD BE FUNDED.

SO THE RECOMMENDATION, AGREED, IS A LITTLE

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COMPLEX AND NUANCED, BUT WE WANTED TO AT LEAST OFFER IT AS A POSSIBILITY. YOU CAN, OF COURSE, DO WHATEVER YOU'D LIKE IN TERMS OF CHOOSING TO FUND WHICHEVER APPLICATIONS.

MR. TORRES: THANK YOU, MR. CHAIRMAN. I THINK IN THE FUTURE, IT WOULD BE A GOOD IDEA FOR YOU TO CONSULT WITH THE CHAIR SO THAT HE AND PERHAPS OTHER MEMBERS ARE AWARE IF THERE'S BEEN ANY CHANGE. THAT WOULD BE AN APPROPRIATE STEP TO TAKE, TALK TO THE CHAIR.

AND SO I MOVE TO APPROVE THE FIRST TWO, WHICH IS TRANS --

MR. SHEEHY: CAN I RULE THAT MOTION OUT OF ORDER?

MR. TORRES: WHY?

MR. SHEEHY: BECAUSE FIRST WE TYPICALLY DEAL WITH THE APPLICATIONS THAT HAVE NOT BEEN RECOMMENDED. WE ALWAYS DO IT --

MR. TORRES: RIGHT. RIGHT. YOU'RE RIGHT. SO MY QUESTION IS HOW MANY MEMBERS FOR THE TWO THAT ARE RECOMMENDED BE APPROVED, HOW MUCH IS LEFT?

MR. SHEEHY: I PERSONALLY WOULD RECOMMEND THE THIRD, PROGRAMMATIC CONSIDERATION. I WOULD LIKE TO SEE CONSIDERED BY THE BOARD, AND THAT'S WHY I'M KIND OF CONFUSED BY THIS PROCESS BECAUSE

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PROGRAMMATIC CONSIDERATIONS ARE NOT BEING BROUGHT TO BEAR ON THIS, ESPECIALLY IN THE CONTEXT OF THE ALMOST $20 MILLION THAT WE'VE RECOVERED, SO WE DO HAVE A LOT OF PEOPLE INTERESTED IN WHAT'S GOING ON HERE. AND IT JUST IS AWKWARD FOR ME, FOR AN AGENCY THAT'S BEEN AROUND FOR THIS LONG, NOT TO BE ABLE TO PRESENT ITSELF WITH A COHERENT, UNITED MESSAGE AND FORMAL COMMUNICATION.

SO, FIRST, IF I COULD, WITH ALL RESPECT TO SENATOR TORRES, ASK IF THERE'S ANY MOTION FROM ANY MEMBER OF THE COMMITTEE TO MOVE ANY APPLICATION FROM TIER II -- AND CAN WE KIND OF MOVE THAT UP BECAUSE I THINK WE NEED TO LET EVERYBODY IN THE CROWD KNOW IN CASE THERE'S SOMEONE HERE WHO WANTS TO SPEAK TO ANY APPLICATION IN TIER II.

IS THERE A MOTION TO RECOMMEND ANY APPLICATION IN TIER II, RECOMMEND THAT IT BE MOVED INTO TIER I? AND IF THERE'S NOT, IS THERE ANY PUBLIC COMMENT? BECAUSE I WANT TO MAKE SURE THAT WE GIVE THE FOLKS THAT ARE HERE TODAY, IF THEY WISH TO SPEAK TO ANY OF THOSE APPLICATIONS, THAT THEY BE GIVEN AN OPPORTUNITY TO DO SO.

TIER II, THE ONES IN WHITE. AND THEN IF THERE'S NOT, COULD I GET A MOTION TO -- SO MAYBE WE SHOULD DO IT IN THE CONTEXT OF A MOTION JUST TO BE

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COMPLETELY COHERENT WITH OUR PROCESSES. CAN WE GET A MOTION NOT TO FUND THE APPLICATIONS IN TIER II?

MR. TORRES: YES.

MR. SHEEHY: SECOND?

CHAIRMAN THOMAS: SECOND.

MR. SHEEHY: AND THEN CAN WE -- WOULD YOU LIKE TO SPEAK TO THAT MOTION? YEAH, PLEASE.

DR. NICHOLAS: THANK YOU FOR THE OPPORTUNITY. MY NAME IS CORY NICHOLAS. I'M THE PI ON TRAN1 PROPOSAL FOR EPILEPSY, AND WE ARE THE ONLY PROPOSAL HERE FOR EPILEPSY. AND I WANT TO MAKE THREE POINTS. AND NOW MY FIRST OF THREE.

MR. SHEEHY: BEFORE YOUR TIME STARTS, CAN WE GET THE NUMBER FOR THAT SO EVERYBODY KNOWS?

DR. NICHOLAS: IF YOU TO SCROLL DOWN, I THINK IT'S THE --

DR. SAMBRANO: IT'S 11611.

MR. SHEEHY: YEAH, PLEASE. SORRY.

DR. NICHOLAS: SO I'D LIKE TO MAKE THREE IMPORTANT POINTS. THE FIRST IS THAT WE ARE THE ONLY PROGRAM IN THE CIRM PORTFOLIO ACTIVELY PURSUING EPILEPSY. EPILEPSY IS THE FOURTH MOST COMMON NEUROLOGICAL DISORDER. IT AFFECTS THREE MILLION AMERICANS AND OVER HALF A MILLION CALIFORNIANS. A THIRD OF THESE FOLKS HAVE NO CURRENT TREATMENT

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OPTION. DRUGS DO NOT WORK. WE WERE PAINFULLY REMINDED RECENTLY WITH THE DISNEY STAR THAT JUST DIED FROM EPILEPSY, AND SOMEONE IN OUR LAB LAST MONTH HAD JUST DIED FROM EPILEPSY. IT'S TRAGIC. AND WHEN IT'S NOT FATAL, IT'S SEVERELY DISABLING. FOLKS CANNOT DRIVE, THEY CANNOT HOLD DOWN A JOB, THEY CANNOT LIVE INDEPENDENTLY. AND WE ARE THE ONLY ACTIVE PROGRAM PURSUING EPILEPSY.

A SECOND POINT IS THAT WE RECEIVED GENEROUSLY A QUEST AWARD TWO YEARS AGO FROM CIRM TO SEE IF OUR HUMAN PRODUCT CANDIDATE WOULD WORK IN RELEVANT ANIMAL MODELS OF EPILEPSY, AND WE CRUSHED THE BALL OUT OF THE PARK. WE EXECUTED ALL OF OUR MILESTONES AHEAD OF SCHEDULE SUCCESSFULLY, AND THIS WAS NOT A MINOR RESPONSE. THIS WAS A COMPLETE CURATIVE RESPONSE, SEIZURE ELIMINATION IN MOST OF THE ANIMALS THAT WE TREATED. SO THIS WAS A DRAMATIC EFFECT. AND IT'S HARD TO IMAGINE THAT WE COULD DO BETTER.

AND, THIRD, WITH THIS DRAMATIC EFFECT THAT WE DEMONSTRATED AND WITH SUPPORT FROM CIRM IN DESIGNING THE ACTIVITIES IN OUR CURRENT TRAN PROPOSAL, WE RESPECTFULLY SCORED VERY WELL. WE ARE A MERE EIGHT OR SEVEN POINTS BELOW THE FUND LINE. AND I WANT TO COMMENT ON WHY WE THINK WE ARE

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UNFAIRLY SCORED.

THE FINAL SHEET FROM THE GRANTS WORKING GROUP WAS THAT WE DIDN'T PROVIDE FULL DISCLOSURE OF OUR MANUFACTURING PROCESS. AND I WANT TO SAY THAT WE ARE THE ONLY COMPANY UP HERE FOR CONSIDERATION. OUR BOARD WOULD NOT ALLOW US TO DISCLOSE THE MANUFACTURING DETAILS. SHORT OF THAT, THE CATEGORIES THAT WE WERE PURSUING IN THIS PROPOSAL, AND WE URGE THE COMMITTEE TO RECONSIDER THIS VOTE. AND WE ASK THAT IF FUNDS ARE PERMITTING, IT APPEARS THAT THERE ARE UNALLOCATED AMOUNTS, YOU CONSIDER FUNDING THIS PROPOSAL OR AT LEAST PUTTING US IN THE WAITING POOL FOR CONSIDERATION WHEN THE UNALLOCATED FUNDS ARE RELEASED. WE REALLY APPRECIATE THE OPPORTUNITY.

MR. SHEEHY: THANK YOU. ARE THERE ANY BOARD COMMENTS OR QUESTIONS?

DR. MARTIN: WOULD EVERYONE WHO IS NOT SPEAKING PLEASE TURN OFF THEIR SPEAKER OR MUTE THEIR PHONE? THE BACKGROUND NOISE IS HORRENDOUS. THANK YOU. THAT MADE A DIFFERENCE.

DR. DULIEGE: I HAVE A QUESTION. CAN SOMEONE FROM THE GRANTS WORKING GROUP OR REPRESENTATIVE PROVIDE SOME EXPLANATION OR RESPONSE TO THE INTERVENTION WE JUST HEARD?

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DR. NICHOLAS: COULD YOU CLARIFY YOUR QUESTION?

MR. SHEEHY: I THINK SHE'S ASKING FOR SOME CLARIFICATION FROM THE GRANTS WORKING GROUP RESPONSE. I THINK THE KEY POINT WAS THAT THE MANUFACTURING PROCESS WAS NOT -- WAS THE MAJOR NEGATIVE POINT, AND THAT WAS INDEED -- IF I PARAPHRASE THIS WRONG, EITHER THE APPLICANT OR DR. DULIEGE IS WELCOME TO CORRECT ME, BUT THAT WAS THE ISSUE, IN THAT IT REQUIRED INFORMATION THAT THEY DID NOT FEEL LIKE THEY WERE ABLE TO DIVULGE.

DR. SAMBRANO: RIGHT. SO THAT IS CORRECT. THE GRANTS WORKING GROUP FELT THAT, AT LEAST FOR THE MANUFACTURING ASPECT, THEY WERE NOT REALLY ABLE TO ASSESS THIS BECAUSE THERE WERE VERY FEW DETAILS THAT WERE PROVIDED. WE GO THROUGH A PROCESS WHERE THE REVIEWERS ARE ALLOWED TO ASK THE APPLICANT QUESTIONS. AND SO THAT QUESTION WAS ASKED OF THE APPLICANT. THE APPLICANT PROVIDED SOME ADDITIONAL DETAILS, BUT NOT SUFFICIENT TO SATISFY THE GRANTS WORKING GROUP.

I WILL POINT OUT THAT THERE ARE, IN FACT, OTHER COMPANIES THAT ARE REPRESENTED AMONG THOSE OF THE 19 THAT APPLIED. AND GENERALLY THE GRANTS WORKING GROUP IS USED TO SEEING MORE DETAIL WITHIN

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THE MANUFACTURING PROCESS.

THERE ARE OTHER ASPECTS OF THE PROPOSAL, HOWEVER, THAT ALSO WERE KEY IN TERMS OF THEIR DECISION. IT WAS NOT SOLELY BASED ON THIS. I THINK REVIEWERS FELT THAT IF OTHER ASPECTS OF THE PROPOSAL WERE HIGHLY MERITORIOUS, THAT THIS PROBABLY WOULD NOT HAVE BEEN SOMETHING THAT THEY WOULD HAVE PREVENTED IT FROM BEING IN THE RECOMMENDED POOL. PART OF THAT WAS JUST CLARITY AROUND THE OVERALL PATIENT BENEFIT AND TRUE CLINICAL GOAL THAT THEY'RE TRYING TO ACHIEVE WITH THIS TREATMENT AND MORE DETAILS ON THEIR OVERALL DEVELOPMENT PLAN AND PROGRAM FOR THIS PRODUCT.

SO THOSE WERE JUST SOME OF THE HIGHLIGHTS OF WHERE THE GRANTS WORKING GROUP WAS THINKING ABOUT THIS APPLICATION.

DR. DULIEGE: THANK YOU VERY MUCH.

WHAT WAS THE SCORE OF THIS APPLICATION?

DR. SAMBRANO: THIS APPLICATION SCORED A 78. THAT WAS THE MEDIAN SCORE. THE AVERAGE WAS 76.

DR. DULIEGE: THANK YOU. CAN THE APPLICANT ADDRESS THE CONCERN THAT WE EXPRESSED TO THEM AND REAPPLY?

DR. NICHOLAS: SORRY. CAN YOU REPEAT THE QUESTION PLEASE?

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DR. DULIEGE: THE QUESTION IS CAN THE APPLICANT ADDRESS THE CONCERNS THAT WERE EXPRESSED TO THE APPLICANT AND REAPPLY LATER?

MR. SHEEHY: THE QUESTION WAS CAN YOU ADDRESS THE CONCERNS AND REAPPLY LATER.

DR. NICHOLAS: MY UNDERSTANDING IS THIS IS THE LAST ROUND.

MR. SHEEHY: YOU'RE RIGHT ABOUT THAT.

DR. NICHOLAS: WE DON'T HAVE ANOTHER CHANCE. THE MANUFACTURING PROCESS IS EXTREMELY SENSITIVE FOR COMPANIES, AS YOU WOULD IMAGINE, AT THIS EARLY STAGE OF DEVELOPMENT. ULTIMATELY, ONCE THIS GETS TO THE FDA, THE PROCESS NEEDS TO BE FULLY DISCLOSED. BUT AT THIS EARLY TRAN STAGE, WE FEEL THAT THE PROCESS IS SO SENSITIVE THAT, IN ORDER TO GENERATE THE HUNDREDS OF MILLIONS OF DOLLARS IN THE FUTURE TO TAKE US ALL THE WAY TO COMMERCIALIZATION, WE NEED TO MAKE SURE WE PROTECT THAT. AND WE DIDN'T FEEL AT THIS TIME WE WANTED TO DISCLOSE THE KEY TRADE SECRETS THAT ARE PART OF THIS PROCESS. AND THAT WAS THE MAIN CRITIQUE. IT'S HARD TO IMAGINE THAT WE COULD DO ANY BETTER WITH OUR RESPONSE IN THIS THERAPY.

BY THE WAY, THIS IS AN INHIBITORY NEURON THERAPY THAT'S VERY UNIQUE IN THAT IT'S POSTMITOTIC.

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WE'VE DEMONSTRATED IT TO BE SAFE. IT INTEGRATES AND PERSISTS, AND WE'VE SHOWN COMPLETE SEIZURE SUPPRESSION. AND SO WE ARE VERY WELL POSITIONED TO TAKE THIS ALL THE WAY, AND I WOULD HATE TO HAVE CIRM DROP THIS AT THIS POINT.

MR. SHEEHY: I JUST HAD ONE QUESTION. WHAT'S THE COMPETITION IN THIS SPACE? LIKE WHAT ARE PEOPLE DOING NOW?

DR. NICHOLAS: RIGHT. SO THERE ARE A LOT OF OBVIOUSLY SMALL MOLECULE DRUGS THAT AREN'T WORKING. A PATIENT IS CONSIDERED TO BE DRUG RESISTANT IF THEY FAIL TWO OR MORE ANTI-EPILEPTIC DRUGS, WHICH IS OFTEN THE CASE. ONCE YOU FAIL TWO DRUGS, YOU HAVE LESS THAN, I THINK, A 5-PERCENT CHANCE OF EVER BENEFITING FROM A FUTURE OR CURRENT DRUG TRIAL.

THERE ARE ALWAYS, OF COURSE, NEW SMALL MOLECULES BEING DEVELOPED. CURRENTLY THE ONLY REAL OPTION FOR PATIENTS WHO HAVE FAILED MULTI DRUGS IS TO HAVE A MASSIVE PIECE OF THE BRAIN REMOVED. FOR THAT REASON, IT'S NOT PURSUED. LESS THAN 10 PERCENT OF PATIENTS WHO ARE ELIGIBLE FOR THIS ACTUALLY GO THROUGH WITH IT BECAUSE YOU RISK PERMANENT COGNITIVE IMPAIRMENTS. AND SO IN THIS WAY WE ARE PROPOSING A RESTORATIVE TREATMENT TO TRY TO ADDRESS THESE -- TO

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RESTORE, THAT IS, TO ABLATE AND DESTROY A MAJOR PIECE OF BRAIN TISSUE. SO THERE REALLY IS NOTHING ELSE.

MR. SHEEHY: WE HAVE ANY ADDITIONAL PUBLIC COMMENT HERE IN SAN FRANCISCO?

DR. KRIEGSTEIN: THANK YOU. I APPRECIATE THE OPPORTUNITY TO SPEAK TO THE COMMITTEE.

I'M ARNOLD KRIEGSTEIN. I DIRECT THE STEM CELL PROGRAM AT UCSF. I WANT TO GIVE THE HISTORY OF THE PROJECT YOU JUST HEARD ABOUT BECAUSE IT STARTED AT UCSF, AND CIRM BEGAN INVOLVEMENT MANY YEARS AGO, SEVEN OR EIGHT YEARS AGO, MAYBE EVEN MORE, WHEN WE TRIED TO DEVELOP HUMAN CELLS THAT COULD BE USED FOR EPILEPSY IN THE ANIMAL MODELS THAT ANIMAL CELLS HAD WORKED IN. AND THAT WAS A CIRM-SPONSORED PROJECT, AND CORY WAS A POST-DOC IN MY LAB, THE FELLOW YOU JUST HEARD FROM JUST NOW, AT THE TIME. AND IT TOOK A NUMBER OF YEARS, BUT WE DID DEVELOP A PROTOCOL FOR MAKING THESE CELLS. AND AS AN ACADEMIC ACTIVITY, THIS WAS, OF COURSE, PUBLISHED AND DISCLOSED. IT BECAME THE FOUNDATION OF THE EFFORT TO ACTUALLY BEGIN MOVING TOWARD THE CLINIC. AND THAT OBVIOUSLY INVOLVED SCALING UP THE PRODUCTION AND DOING IT THROUGH GMP FACILITIES AND CHANGING OF THOSE GROWTH FACTORS TO SMALL MOLECULES AND DOING ALL THE

SCALING-UP ACTIVITIES THAT ARE NOT REALLY DONE IN AN ACADEMIC SETTING.

AND SO IT WAS AT THAT POINT THAT WE STARTED THIS COMPANY, AND IT WAS MOVED TO SOUTH SAN FRANCISCO. CORY BECAME THE CHIEF SCIENTIFIC OFFICER, AND THE PROJECT CONTINUED TO FLOURISH IN THAT SETTING. IT BECAME, I THINK, A VERY SUCCESSFUL EXAMPLE OF HOW YOU TRANSITION FROM WHAT STARTED AS AN ACADEMIC ENTERPRISE INTO SOMETHING THAT REALLY IS MOVING TOWARD THE CLINIC AND BECOMING A PRODUCT.

OF COURSE, WHEN THAT HAPPENED, THE PROTOCOL FOR MAKING THE CELLS WAS TWEAKED. IN FACT, IT WAS VERY SIGNIFICANTLY IMPROVED. THE PURITY OF THE CELLS, WHICH WERE 40 TO 60 PERCENT IN MY LAB, ARE NOW 99 PERCENT OR BETTER. THEY'RE ALL POSTMITOTIC. THEY'RE GENERATED THROUGH ALL GMP PRODUCTS, AND THE SCALING-UP PROCESS IS COMPATIBLE WITH BIOREACTORS. ALL THE GOALS THAT THE COMPANY HAD IN MIND HAVE BEEN ACHIEVED. AND AS YOU HEARD THROUGH CIRM, WE WERE ABLE TO USE THESE CELLS IN ANIMAL MODELS AND SHOW REALLY A SURPRISE, A SHOCKING DEGREE OF IMPROVEMENT. SO WE FEEL AS THOUGH THIS PROJECT HAS MOVED EXACTLY THE WAY IT SHOULD AND IS MOVING VERY NICELY TOWARD THE CLINIC. AND SO THAT'S WHY I FEEL IT WAS AN UNFAIR CRITICISM THAT WE

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WEREN'T FULLY DISCLOSING OUR MANUFACTURING PROCESS.

MR. SHEEHY: THANK YOU, DR. KRIEGSTEIN. I HAVE A QUICK QUESTION. SO ARE THESE CELLS DERIVED FROM -- IS THIS TECHNOLOGY EMBRYONIC STEM CELL BASED?

DR. KRIEGSTEIN: YES. IT STARTS WITH AN EMBRYONIC STEM CELL LINE. IT'S A SINGLE PRODUCT. SO WE'VE CHOSEN ONE LINE TO MAKE OUR CELLS.

MR. SHEEHY: I THINK WE'RE GOING TO END UP WITH APPLICATIONS OPEN. I WONDER IF THE MAKERS OF THE MOTION WOULD ACCEPT A FRIENDLY AMENDMENT TO HOLD THIS APPLICATION OPEN.

MR. TORRES: VERY FRIENDLY, I HOPE.

MR. SHEEHY: TO HOLD THIS APPLICATION TO INCLUDE IN THIS MOTION TO NOT FUND THE APPLICATIONS IN TIER II WITH THE EXCEPTION THAT THIS ONE, WHICH IS 11611, BE HELD OPEN FOR FURTHER DISCUSSION IF OTHER FUNDS BECOME AVAILABLE.

MR. TORRES: WE ARE FINE.

MR. SHEEHY: YOU'RE BOTH FINE WITH THAT? SO PERHAPS IN THE MEANTIME WE CAN MAYBE HAVE A LITTLE BIT OF DIALOGUE BECAUSE I KNOW THIS IS A HUGE UNMET NEED. AND, FRANKLY, JUST TO KIND OF PREFIGURE WHERE I'M COMING FROM TODAY, IS THAT I DO THINK THAT AS WE GET TO THE LAST OF OUR MONEY, A RENEWED AND

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FOCUSED -- A RENEWED FOCUS ON WHAT LIES BEHIND -- UNDERNEATH OUR FOUNDING, WHICH IS EMBRYONIC STEM CELL TECHNOLOGY, WHICH WE'VE LED THE WORLD ON, I WOULD SAY, AND WE HAVE, IN RELATION TO WHAT WE'VE BEEN DOING, A RELATIVELY LOW YIELD IN THAT PARTICULAR TECHNOLOGY, THAT WE DOUBLE DOWN HERE WITH OUR REMAINING FUNDS.

SO WITH THAT BASIS --

MR. TORRES: MOVE AS AMENDED.

MR. SHEEHY: MOVED AS AMENDED. CAN WE CALL THE ROLL.

CHAIRMAN THOMAS: SECOND AS AMENDED.

MS. BONNEVILLE: CAN I HAVE A CLARIFICATION JUST FOR THE MOTION? IS THIS TO HOLD IT OPEN TO THEN CONSIDER LATER OR IN ADDITION TO THE ONES THAT YOU'RE GOING TO BE TAKING UP AFTER?

MR. SHEEHY: YEAH. TO HOLD IT OPEN WITH ONES THAT WE WILL HOLD OVER. PRESUMABLY WE WILL HOLD OPEN WITHIN THE TIER I.

MS. BONNEVILLE: OKAY. GREAT. THANK YOU.

MR. TORRES: I PRESUME YOU'RE GOING TO THANK YOUR PROFESSOR.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.
MS. BONNEVILLE: STEVE JUELSGAARD.
MR. JUELSGAARD: YES.
MS. BONNEVILLE: DAVE MARTIN.
DR. MARTIN: YES.
MS. BONNEVILLE: ADRIANA PADILLA.
DR. PADILLA: YES.
MS. BONNEVILLE: JOE PANETTA. JOE PANETTA. FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: YES.
MS. BONNEVILLE: AL ROWLETT. JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR. JOE PANETTA.
MR. PANETTA: YES.
MS. BONNEVILLE: THANK YOU.
MR. PANETTA: SORRY.
MS. BONNEVILLE: NO PROBLEM. DIANE AND AL ARE THE LINE? DIANE AND AL, I BELIEVE YOU BOTH ARE

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ON MUTE.

MS. WINOKUR: YES.

MS. BONNEVILLE: THANK YOU, DIANE. HOW ABOUT AL? OKAY. MOTION CARRIES. IS THAT AL?

MR. ROWLETT: YES. SORRY.

MS. BONNEVILLE: THANK YOU.

MR. SHEEHY: NOW WE HAVE THE GROUP IN TIER I. SO, SENATOR TORRES, IF YOU WANTED TO MAKE YOUR MOTION.

MR. TORRES: OH, THANKS. I MOVE TO APPROVE THE TWO IN TIER I.

MR. SHEEHY: IS THERE A SECOND?

CHAIRMAN THOMAS: SECOND.

MR. SHEEHY: SO I'D LIKE TO SPEAK AGAINST THAT MOTION. IN MY VIEW, WE HAVE THREE EMBRYONIC STEM CELL-BASED THERAPIES IN THIS ROUND AND ONE FETAL TISSUE THERAPY. WE KNOW THE REASON THIS AGENCY WAS FUNDED WAS TO FUND EMBRYONIC STEM CELL THERAPIES, AND WE KNOW THAT THE FEDERAL GOVERNMENT IS LOOKING ASKANCE AT FETAL TISSUE RESEARCH. AND THIS GOES TO THE HEART OF WHY CIRM EVEN EXISTS, WHY WE HAVEN'T DECIDED AS A STATE TO RELY ON THE FEDERAL GOVERNMENT.

THOSE APPLICATIONS ARE 11532, 11579, 1148 THOSE ARE THE EMBRYONIC STEM CELL-BASED

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APPLICATIONS. AND 11628 IS THE FETAL TISSUE-BASED THERAPY. IF I'M INCORRECT, I HOPE THAT REPRESENTATIVES OF THE APPLICANTS WILL CORRECT ME.

I'M SPEAKING TO THE MOTION. I'M NOT MAKING A MOTION.

MS. BONNEVILLE: OKAY.

UNIDENTIFIED SPEAKER: 11544 IS ALSO FETAL STEM CELLS.

MR. SHEEHY: THERE ARE TWO FETAL, 11544. OF THE FOUR THAT I SELECTED, I JUST NOTE THERE IS EXACTLY $20 MILLION.

MS. BONNEVILLE: A COINCIDENCE.

MR. SHEEHY: A COINCIDENCE AS THEY KIND OF ADD UP TO THAT. EVEN THOUGH I'M VERY SUPPORTIVE OF THAT APPLICATION, I DON'T SEE WHY WE COULDN'T HOLD IT.

ANYWAY, THAT'S JUST WHY I'M NOT GOING TO BE SUPPORTIVE OF THIS BECAUSE I THINK, AS WE GET TO LOWER FUNDS, AND I WOULD NOTE THAT FIVE OF THE TOP SIX APPLICATIONS, AS WE GET TO HAVING LESS FUNDS, THAT WE SHOULD PRIORITIZE THOSE APPLICATIONS THAT ARE MOST ALIGNED WITH THE ORIGINAL REASON FOR THE ESTABLISHMENT OF THIS AGENCY.

OTHER BOARD COMMENTS ON THE MOTION TO APPROVE THE FIRST TWO ARE WELCOME.

MR. TORRES: MY MOTION?

MR. SHEEHY: YES.

MR. TORRES: I WOULD ARGUE THAT IN DEALING WITH WHAT CIRM'S LEGACY SHOULD BE, IT SHOULD ALSO BE REFLECTIVE OF THE PATIENTS THAT WE WANT TO IMPACT WITH OUR RESEARCH AND WITH OUR FUNDING. AND CLEARLY IN MY MIND MACULAR DEGENERATION, DRY MACULAR DEGENERATION, AFFECTS DISPROPORTIONATELY THOSE PEOPLE OVER SIXTY.

MR. SHEEHY: WE ARE ALIGNED ON THAT APPLICATION.

MR. TORRES: WE ARE. OKAY. WELL, THEN, I'M ALIGNED EVEN MORE.

MR. JUELSGAARD: MR. SHEEHY, THIS IS STEVE JUELSGAARD.

MR. SHEEHY: YES, PLEASE.

MR. JUELSGAARD: SO I WOULD LIKE TO JUST BACK UP A MINUTE AND ASK DR. SAMBRANO WHAT WAS THE BASIS, THE PRIMARY BASIS, FOR THE STAFF'S RECOMMENDATION THAT WE APPROVE THE APPLICATIONS ENDING IN 36 AND 32? WHAT WAS THE TIPPING POINT THAT SAID DEFINITELY --

MR. SHEEHY: DID WE LOSE YOU, STEVE?

(PAUSE IN PROCEEDINGS.)

(047:44) MR. JUELSGAARD: THIS IS STEVE

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JUELSGAARD AGAIN. FOR SOME REASON I JUST GOT KICKED OFF THE PHONE. SO I HOPE MY QUESTION CAME THROUGH.

MS. BONNEVILLE: CAN YOU PLEASE RESTATE, STEVE?

MR. JUELSGAARD: YES. THIS IS A QUESTION FOR DR. SAMBRANO. SO WHAT WAS THE MAJOR REASON OR REASONS FOR THE RECOMMENDATIONS OF THE TWO APPLICATIONS THAT HE IDENTIFIED THAT THE STAFF IS RECOMMENDING FOR APPROVAL? WHAT WAS DIFFERENT ABOUT THEM THAN THE OTHER APPLICATIONS THAT RESULTED IN THAT RECOMMENDATION?

DR. SAMBRANO: SURE. SO JUST TO BE CLEAR, WE AREN'T MAKING ANY PROGRAMMATIC RECOMMENDATION WHATSOEVER. SO THE RECOMMENDATION THAT WE ARE MAKING IS SOLELY BASED ON THE SCORE AND BASED ON THE FACT THAT WE THINK ALL OF THE APPLICATIONS HAVE MERIT. AND IT WAS A MATTER OF SUGGESTING THAT AT LEAST FOUR APPLICATIONS BE APPROVED TODAY AND THE OTHERS BE HELD OVER FOR POSSIBLE FUNDING IN SEPTEMBER. SO OUR GOAL ULTIMATELY WAS TO ACTUALLY HAVE FUNDING FOR ALL SEVEN. THE STRATEGY WAS JUST SIMPLY HOW TO ADD UP UP TO 20 IN GOING DOWN THE RANK ORDER.

MR. JUELSGAARD: RIGHT. SO AS I UNDERSTAND IT, THE PRINCIPAL BASIS FOR THE

RECOMMENDATION WAS THE SCIENTIFIC SCORE AND NOTHING BEYOND THAT, NOTHING PROGRAMMATIC.

DR. SAMBRANO: CORRECT.

MR. JUELSGAARD: OKAY. SO THIS HAS BEEN, I THINK, WHERE WE REALLY COME INTO THE MIDDLE OF WHAT NEEDS TO BE DONE HERE; THAT IS, THIS GROUP, THE APPLICATION REVIEW SUBCOMMITTEE, AND THAT'S THE PROGRAMMATIC REVIEW, WHICH TO ME IS A DIFFERENT WAY OF LOOKING AT THINGS THAN SCIENTIFIC MERIT. BECAUSE FOR ME, ONCE SOMETHING HAS A SCORE OF 85 OR GREATER, IT HAS SCIENTIFIC MERIT, AND I TEND TO DISCOUNT THE DIFFERENCE IN SCORES AS BEING ALL THAT SIGNIFICANT AND, INSTEAD, TEND TO LOOK AT THE INDICATION.

SO JEFF WANTS TO LOOK AT THE, IN ESSENCE, THE CONNECTION TO REGENERATIVE MEDICINE, WHAT IS THAT, WHICH IS FINE. I DON'T HAVE AN ARGUMENT WITH THAT. THAT'S ONE WAY OF LOOKING AT IT.

ANOTHER WAY OF LOOKING AT IT IS TO SAY WHAT ARE THE INDICATIONS THAT THESE PARTICULAR POTENTIAL THERAPEUTICS THAT ARE IN TRANSLATION, WHAT ARE THEY AIMED AT, AND HOW IMPORTANT ARE THOSE POTENTIAL DISEASES THAT THEIR THERAPY IS FOR, AND WHAT ELSE EXISTS OUT THERE RIGHT NOW BOTH WITHIN OUR OWN PORTFOLIO, BUT ALSO OUTSIDE OF OUR OWN PORTFOLIO, THAT ARE AIMED AT LOOKING AT THESE SORTS

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OF PROBLEMS?

AND SO WHILE I HAVE MY OWN POINTS OF VIEW ABOUT WHAT -- HOW I WOULD RANK THESE IN TERMS OF IMPORTANCE FROM WHAT I CALL A THERAPEUTIC POINT OF VIEW, I WOULD SUGGEST THAT, AS WE THINK THROUGH THIS, EACH OF US INDIVIDUALLY, THAT THAT MIGHT BE ONE WAY THAT WE LOOK AT THIS AND THINK ABOUT IT IS WHAT OF THESE DISEASES ACTUALLY NEEDS THE MOST SUPPORT AT THIS POINT OF VIEW BECAUSE THEY'RE THE MOST PROBLEMATIC DISEASES WE HAVE TO DEAL WITH, AT LEAST THAT WE CAN UNDERSTAND OR SEE AT THIS POINT.

MR. SHEEHY: THANK YOU, DR. -- I MEAN MR. JUELSGAARD. CHAIRMAN THOMAS.

CHAIRMAN THOMAS: I THINK HE ACTUALLY IS DR. JUELSGAARD IF YOU COUNT THE VETERINARY ASPECT OF THINGS.

MR. JUELSGAARD: LITTLE KNOWN FACT, YES.

MR. TORRES: I DIDN'T KNOW THAT EITHER.

CHAIRMAN THOMAS: FURTHER TO DR. JUELSGAARD'S COMMENTS, DR. SAMBRANO, COULD YOU SPEAK A BIT TO THE PREVALENCE IN THE PORTFOLIO OF OTHER, AS WE DO ON THE CLINS, OTHER PROJECTS IN RELATION TO WHAT'S LISTED HERE AMONGST THESE SEVEN?

DR. SAMBRANO: I CAN.

CHAIRMAN THOMAS: BY THE WAY, WHILE YOU'RE

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AT IT, PUT THE EPILEPSY BACK FOR CONSIDERATION, AT SOME POINT SPEAK TO THAT ON THE SAME QUESTION AS WELL.

MR. SHEEHY: WELL, MAYBE -- THAT'S ONE THING. MAYBE IF I COULD STEP INTO THE MIDDLE OF THIS QUESTION. COULD WE -- I DON'T KNOW IF WE'D LIKE TO DO A MOTION, OR COULD WE AGREE AS A GROUP THAT INCLUDED IN OUR RECOMMENDATION, WHATEVER FINAL MOTIONS WE DO, WE WILL REQUEST THAT THE REMAINING APPLICATIONS BE HELD OPEN IN THE EVENT THAT THE FULL BOARD IN SEPTEMBER MAKES THE DECISION TO ALLOCATE PART OF THE WHAT IS NOW 20 MILLION AND MAYBE A BIT MORE BY THEN IN RETURNED FUNDS? IF THIS BODY FEELS COMFORTABLE -- IF THERE'S ANY OBJECTION TO THAT, WE CAN KIND OF DO A MOTION; BUT, OTHERWISE, WE CAN ADD IT TO WHATEVER OUR FINAL MOTION IS. IF EVERYBODY IS COMFORTABLE WITH THAT. WE'RE CLEAR WE'RE GOING TO TRY TO FUND ALL THESE.

MS. WINOKUR: MAY I ASK A QUESTION?

MR. SHEEHY: SURE.

MS. WINOKUR: THE APPLICATIONS THAT WE HOLD OPEN, WHAT IS THE GROUP? WILL THEY JUST COMPETE AGAINST EACH OTHER THE NEXT TIME AROUND? WILL THEY BECOME PART OF THE NEW GROUP OF APPLICATIONS THAT COME IN AND COMPETE WITH THEM?

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MR. SHEEHY: MS. WINOKUR, WHAT WOULD HAPPEN, AND THIS IS WHAT WE DID THE LAST TIME WE HAD AN EXCESS OF TRANSLATION APPLICATIONS OR MAYBE IT WAS QUEST IS THAT WE HELD THEM OPEN. WHEN THE BOARD RELEASED THE NEXT TRANCHE OF FUNDS, THEN THE APPLICATION REVIEW COMMITTEE MET TO APPLY THOSE FUNDS TO THOSE APPLICATIONS. THERE WAS NO NEED TO COME BACK IN FOR ANOTHER COMPETITION. THEY WERE NOT RESCORED. THE BOARD APPLIED THE FUNDS THAT HAD BECOME AVAILABLE TO THOSE APPLICATIONS AND THEY WERE FUNDED.

THE ROUGH DELAY IN THIS CASE WOULD BE ABOUT THREE MONTHS, I THINK, IN TERMS OF FUNDING?

MS. BONNEVILLE: IT FIRST WENT TO THE FULL BOARD TO DETERMINE THAT THAT SORT OF MONEY WOULD BE ALLOCATED. SO WE DID IT AT A MEETING WHERE THE FULL BOARD MET, AND THEN SUBSEQUENTLY YOU WENT INTO THE APPLICATION REVIEW SUBCOMMITTEE TO THEN APPLY THOSE FUNDS.

MR. SHEEHY: RIGHT. SO THAT'S THE PROCESS.

MR. TORRES: SO WHAT IS ON THE TABLE NOW? IS THERE A MOTION THAT'S ALIVE ON THE TABLE NOW?

MR. HUANG: YES.

(SIMULTANEOUS DISCUSSION.)

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MR. TORRES: THIS IS THE ONE THAT WE AMENDED WITH THE FRIENDLY AMENDMENT?

MS. BONNEVILLE: WE HAVE AN AMENDMENT.

MR. TORRES: OH, I THOUGHT WE PASSED THAT. OKAY.

MR. HUANG: NO. NO. YOUR INITIAL MOTION WAS TO FUND THE FIRST TWO.

MR. TORRES: CORRECT.

MR. HUANG: AND THEN --

MR. TORRES: WE BECAME FRIENDS.

MR. SHEEHY: I DID MAKE AN AMENDMENT.

MR. HUANG: YOU DID MAKE AN AMENDMENT.

MR. SHEEHY: IF YOU TAKE THAT AS AN AMENDMENT --

MR. TORRES: NO, WE DID. J.T. AND I SAID YES.

MS. BONNEVILLE: THAT WAS THE ONE PRIOR. THAT WAS THE PRIOR ONE.

MR. TORRES: WHAT'S ON THE TABLE NOW?

MS. BONNEVILLE: YOU MADE A MOTION TO FUND THE TOP TWO.

MR. TORRES: OKAY. AND YOU WANTED TO AMEND THAT MOTION AS WELL?

MR. SHEEHY: I WOULD BE HAPPY TO AMEND THAT MOTION TO APPROVE THE FOUR BELOW THE TOP ONE

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BECAUSE THREE OF THOSE -- THE SECOND, THIRD, AND FOURTH ARE EMBRYONIC STEM CELL-DERIVED PRODUCT AND THE FOURTH ONE IS THE FETAL TISSUE-DERIVED PRODUCT, AND THERE'S ONE MORE FETAL TISSUE PRODUCT, BUT I DON'T THINK WE CAN FIT THAT IN WITHIN OUR BUDGET.

DR. PRIETO: CAN I OFFER THAT AMENDMENT?

MS. BONNEVILLE: YOU WANT -- LET ME GET THIS STRAIGHT. YOU WANT TO FUND ONE THROUGH FIVE?

MR. SHEEHY: TWO THROUGH SIX.

MS. BONNEVILLE: TWO, THREE, FOUR, FIVE, SIX. I DON'T KNOW IF THERE'S ENOUGH MONEY FOR THAT.

MR. SHEEHY: TWO THROUGH FIVE.

MS. BONNEVILLE: TWO THROUGH FIVE. SO THAT WOULD BE AMENDING ART AND J.T.'S MOTION.

MR. TORRES: THAT WAS THE FIRST ONE?

MR. SHEEHY: THE FIRST ONE CAN WAIT.

MR. TORRES: I THOUGHT THE FIRST ONE GOES.

MR. HUANG: WOULD IT BE EASIER, THEN, TO WITHDRAW THE MOTION? IF YOU ARE IN CONCURRENCE, WITHDRAW MOTION. THEN --

MR. TORRES: THE FRIENDLY AMENDMENT, IF MY EFFORT TO MAKE SURE THAT 11532 GETS THROUGH --

MS. BONNEVILLE: YES. HE'S SUGGESTING -- HE'S SUGGESTING --

MR. HUANG: THE AMENDMENT WOULD BE AWKWARD

BECAUSE YOUR MOTION IS TO ACCEPT THE FIRST TWO, AND THEN THE AMENDMENT IS TO LEAVE THE FIRST ONE OPEN.

MR. TORRES: MAYBE IF I WITHDRAW MY MOTION AND ENTER A NEW MOTION, IF I MAY DO SO, MR. CHAIR?

MR. SHEEHY: YES.

MR. TORRES: AND MY NEW MOTION IS TO APPROVE 11532 ON ITS OWN, AND THEN YOU CAN ENTERTAIN A MOTION ON YOUR ISSUES.

MR. SHEEHY: WE CAN DO THAT.

MR. TORRES: OR YOU CAN AMEND --

MR. SHEEHY: THAT'S FINE.

MR. HUANG: SO THE MOTION ON THE TABLE IS TO APPROVE TRAN1-11532. IS THERE A SECOND?

MR. SHEEHY: I'LL SECOND.

DR. PRIETO: SECOND.

MR. TORRES: THANK YOU.

MS. BONNEVILLE: ART AND JEFF.

CHAIRMAN THOMAS: MR. CHAIRMAN.

MR. SHEEHY: YES.

CHAIRMAN THOMAS: SO, AGAIN, I WOULD LIKE TO HAVE THE -- AS PART OF WHERE THIS IS HEADED, I'D LIKE TO HAVE, IN CONNECTION WITH THIS, THIS IS AS GOOD A MOTION AS ANY, HAVE DR. SAMBRANO ADDRESS THE QUESTION I ASKED, WHICH I THINK ALSO GETS TO DR. JUELSGAARD'S POINT.

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MR. TORRES: THIS MOTION ONLY HAS TO DEAL WITH ONE APPLICATION.

CHAIRMAN THOMAS: I UNDERSTAND THAT.

MR. TORRES: SO YOU WANT TO RESERVE THE QUESTIONS AFTER I GET MY VOTES?

DR. SAMBRANO: I CAN PROVIDE YOU WITH SOME OF THE PORTFOLIO INFORMATION FOR THIS ONE IF YOU'D LIKE TO AT LEAST JUST FOCUS ON THIS ONE NOW. I CAN ALSO POINT YOU TO THE FACT THAT BEHIND THE MEMO WE ALSO HAD PORTFOLIO INFORMATION FOR THOSE SEVEN TRAN APPLICATIONS THAT SPEAK TO WHAT WE HAVE IN OUR CURRENT PORTFOLIO. SO THAT'S WHERE I'LL HIGHLIGHT THE INFORMATION FROM.

SO IF WE ARE TALKING ABOUT 11532, WE HAVE IN THE CIRM PORTFOLIO NINE ACTIVE AWARDS THAT ADDRESS VISION LOSS, EIGHT THAT ARE FOCUSED ON RETINAL DISEASE, AND ONE ON CORNEAL INJURY. WE HAVE FIVE DEVELOPMENTAL STAGE CELL THERAPIES FOR AMD AND/OR RETINITIS PIGMENTOSA. THOSE ARE TWO CLIN AND THREE TRAN STAGE. WE HAVE TWO DISCOVERY STAGE PROJECTS THAT USE PLURIPOTENT STEM CELLS THAT ARE DERIVING RETINAL TISSUES FOR MODELING RETINAL DISEASE AND/OR EXPLORING RETINAL CELL REPLACEMENT STRATEGIES, ONE DISCOVERY STAGE AWARD THAT IS PURSUING A SMALL MOLECULE THERAPY FOR GENE-SPECIFIC

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PHOTORECEPTOR DISEASE.

BUT THIS PARTICULAR CANDIDATE DIFFERS FROM OTHERS. THIS IS A BIOLOGIC, SO THESE ARE SOLUBLE FACTORS THAT ARE DERIVED FROM THE CULTURE OF HUMAN EMBRYONIC STEM CELL-DERIVED RETINAL PIGMENT EPITHELIAL CELLS. AND SO THOSE SOLUBLE FACTORS ARE BASICALLY THE PRODUCT THAT THEY ARE TRYING TO ADVANCE. SO THAT ITSELF IS A UNIQUE TECHNOLOGY THAT WE ARE NOT FUNDING.

MR. SHEEHY: AND WOULD I BE CORRECT TO SAY THAT THIS IS A TECHNOLOGY THAT'S BEEN DEVELOPED BY CIRM, I BELIEVE --

DR. SAMBRANO: YES, CORRECT.

MR. SHEEHY: SO OTHER BOARD COMMENT ON THIS MOTION? IS THERE PUBLIC COMMENT ON THIS MOTION?

MR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD AGAIN.

MR. SHEEHY: PLEASE.

MR. JUELSGAARD: SO I THOUGHT WHAT DR. SAMBRANO PRESENTED WAS PRETTY ILLUMINATING. I DON'T KNOW HOW MANY OTHER INDICATIONS WE HAVE THAT HAVE SOME MANY -- SO MUCH EFFORT FOCUSED ON THEM IN OUR PORTFOLIO OR AT LEAST EFFORT FOCUSED IN THAT DISEASE AND EYE DISEASES COMPARED SO SOME OF THE OTHERS.

AND I WOULD ALSO SUGGEST THAT THERE'S CERTAINLY A LOT OF EFFORT BEING UNDERTAKEN OUTSIDE OF WHAT CIRM IS DOING IN THE WHOLE PHARMACEUTICAL INDUSTRY ON THIS DISEASE OF AGE-RELATED MACULAR DEGENERATION, THE DRY FORM.

SO IT'S NOT CLEAR TO ME THAT THIS IS THE BEST USE OF OUR FUNDS GIVEN WHAT I THINK IS ALREADY A PLETHORA OF WORK THAT'S GOING ON INTERNALLY AND WITH RESPECT TO OTHERS.

JUST TO TAKE AS AN ALTERNATIVE, BECAUSE WE'VE BEEN -- THIS IS ONE OF THE THINGS WE'VE PRIDED OURSELVES ON. THE APPLICATION THAT ACTUALLY RANKED HIGHER THAN THIS, THE 36 APPLICATION THAT HAS TO DO WITH X-LINKED HYPER IGM SYNDROME, I DARE SAY PROBABLY ALMOST -- BECAUSE IT'S SO RARE, PROBABLY NOBODY ELSE IS WILLING TO FUND SOMETHING LIKE THIS, IS WILLING TO PROVIDE ANY SORT OF TRACTION FOR IT. AND THIS IS THE KIND OF ORGANIZATION THAT'S BEEN WILLING IN THOSE KIND OF SITUATIONS TO STEP INTO THAT LURCH AND PROVIDE SOME FUNDING FOR WHAT ARE TYPICALLY CLEARLY RARE INDICATIONS TO AT LEAST SEE IF SOME PROGRESS CAN BE MADE.

SO, ANYWAY, I GUESS MY POINT IS I AM -- I GUESS I'M NOT IN FAVOR FROM MY POINT OF VIEW OF APPROVING THIS APPLICATION BECAUSE I THINK THERE ARE

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OTHERS THAT ARE ONES THAT WE SHOULD CONSIDER IN FRONT OF THIS FOR OTHER REASONS.

MR. SHEEHY: SO DO WE HAVE ANY OTHER BOARD COMMENTS FOR THIS MOTION? QUESTIONS? DO WE HAVE ANY PUBLIC COMMENT?

DR. HUMAYAN: I'D LIKE TO THANK THE BOARD FOR ALLOWING ME TO SPEAK. I'M MARK HUMAYAN. I'M THE PRINCIPAL INVESTIGATOR ON THIS GRANT. I'M A RETINA SPECIALIST AND BIOMEDICAL ENGINEER.

I THINK CLEARLY MACULAR DEGENERATION NEEDS FURTHER DISCUSSION. THERE ARE TWO TYPES OF MACULAR DEGENERATION. THERE'S THE WET TYPE WHERE THERE WAS BLEEDING THAT OCCURRED, AND CLEARLY THERE'S A LOT OF INDUSTRY, A LOT OF MONEY BEING SPENT ON TREATING THAT, BUT 90 PERCENT OF MACULAR DEGENERATION IS ACTUALLY THE DRY TYPE, NOT THE WET TYPE. AND THIS IS UNRELENTING, AND YOU EVENTUALLY GO BLIND FROM NOT NEW VASCULARIZATION, BUT ATROPHY OF THE RETINAL PIGMENT EPITHELIUM.

SO I THINK TO SAY THAT THERE'S INDUSTRY CHASING AND THERE'S A LOT OF ACTIVITY IN MACULAR DEGENERATION, WE JUST HAVE TO MAKE IT VERY CLEAR THAT THERE ARE TWO DIFFERENT TYPES. AND, YES, IN WET THERE IS; BUT IN DRY, NO. IN FACT, A LOT OF COMPANIES HAVE FAILED IN DRY MACULAR DEGENERATION

BECAUSE THEY'VE TRIED A SINGLE TARGET, EITHER AN ANTI-INFLAMMATORY OR A NEUROPROTECTIVE APPROACH. AND THE ADVANTAGE OF USING THE SOLUBLE FACTORS FOR USING EMBRYONIC STEM CELL-DERIVED RPE IS THAT THEY GIVE YOU A COMBINATION OF BOTH. AND WHAT WE FOUND IS THAT IN AN FDA-APPROVED ANIMAL MODEL, FOR THE VERY FIRST TIME, THAT THIS TYPE OF APPROACH STARTS TO SLOW DOWN THE RETINAL PROBLEMS.

SO THIS IS CLEARLY AN UNMET NEED. THERE'S COST IN CALIFORNIA ALONE MORE THAN $3 BILLION, MORE THAN HALF OF 500,000 EACH YEAR OF PATIENTS WHO SUFFER FROM MACULAR DEGENERATION. IT ADDRESSES A DIFFERENT FORM, WHICH CURRENTLY THERE ISN'T ANY THERAPY FOR. A LOT OF COMPANIES HAVE FAILED BECAUSE THEY'VE TRIED TO DEVELOP MONOTHERAPIES WITH SMALL MOLECULES. THIS IS A WONDERFUL APPROACH AND A REALLY IMPORTANT APPROACH WHERE WE CAN USE CIRM FUNDED -- WE'VE BEEN VERY GRATEFUL TO CIRM FOR FUNDING US -- TO TAKE THIS APPROACH AND USE THE SOLUBLE FACTORS TO MAKE AN ENORMOUS DIFFERENCE IN PATIENTS WITH VISION PROBLEMS.

IF YOU THINK ABOUT IT, WE ALL LIVE TO OUR RETIREMENTS, WE ARE ALL HEALTHY; BUT IF YOU LOSE YOUR VISION, YOU'RE INCREDIBLY INCAPACITATED IF YOU CAN'T READ, RECOGNIZE FACES, WATCH TELEVISION, OR

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DRIVE. SO IT'S USUALLY IMPACTFUL. THIS HAS BEEN FUNDED BY CIRM. IT IS NOT BEING DONE BY OTHER INDUSTRY AND IT'S A HUGE UNMET NEED. SO THANK YOU FOR LETTING ME MAKE THAT COMMENT.

MR. SHEEHY: THANK YOU. SO IF THERE'S NO MORE BOARD COMMENTS OR ANY OTHER PUBLIC COMMENT, WE CAN CALL THE ROLL ON THE MOTION, WHICH IS TO APPROVE 11532.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: NO.

MS. BONNEVILLE: DAVE MARTIN.

DR. MARTIN: YES.

MS. BONNEVILLE: ADRIANA PADILLA.

DR. PADILLA: YES.

MS. BONNEVILLE: JOE PANETTA. 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: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
MS. BONNEVILLE: THANK YOU. MOTION CARRIES.
MR. SHEEHY: SO THAT'S ONE DOWN, AND THAT'S APPROXIMATELY 3.7 MILLION. SO --
DR. PRIETO: MR. CHAIRMAN?
MR. SHEEHY: YES, PLEASE.
DR. PRIETO: CAN I MAKE A MOTION TO APPROVE THE NEXT THREE ON OUR LIST, 11579, 11548, AND 11628?
MR. SHEEHY: YES. AND I WOULD SECOND THAT.
DO WE HAVE ANY DISCUSSION ON THIS MOTION? CHAIRMAN THOMAS.
CHAIRMAN THOMAS: SO I'D JUST LIKE TO HEAR, SINCE THAT WOULD FACTOR IN ONE OF THE FETAL TISSUE PROJECTS AND NOT ANOTHER THAT HAD THE SAME MEDIAN SCORE, WOULD LIKE TO HEAR SORT OF WHAT THE

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DISTINCTION IS AND WHY WE WOULD PROPOSE TO FUND ONE RATHER THAN THE OTHER AT THIS STAGE, UNDERSTANDING THAT EVERYTHING ELSE IS GOING TO BE HELD OVER AND HOPEFULLY FROM THAT PERSPECTIVE (INAUDIBLE). DR. SAMBRANO.

MR. SHEEHY: THIS WAS -- WE MADE --

CHAIRMAN THOMAS: GET A SCIENTIFIC EXPLANATION.

DR. SAMBRANO: I CAN'T PROVIDE A SCIENTIFIC REASON FOR WHY YOU WOULD PICK ONE OVER THE OTHER.

CHAIRMAN THOMAS: REPHRASE THAT. IF YOU COULD JUST GIVE SCIENTIFIC HIGHLIGHTS FOR BOTH.

DR. SAMBRANO: SO THE TWO FETAL ONES THAT WE ARE TALKING ABOUT, 11544, WHICH IS THE LAST ONE, WE JUST DID THE ONCOLYTIC IMMUNOTHERAPY FOR OVARIAN CANCER. THE OTHER ONE WOULD BE THE NEURAL STEM CELLS FOR NEUROPROTECTION IN PERINATAL HYPOXIC ISCHEMIC BRAIN INJURY.

SO LET ME ADDRESS 11628 FIRST. SO IN TERMS OF THE PORTFOLIO, WE DON'T CURRENTLY HAVE ANYTHING IN OUR PORTFOLIO THAT IS ADDRESSING HYPOXIC ISCHEMIC BRAIN INJURY. SO THAT WOULD BE UNIQUE IN OUR PORTFOLIO.

IN TERMS OF THE REVIEW, GIVE ME A MOMENT,

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SO THIS IS AN APPLICATION THAT USES FETAL-DERIVED HUMAN NEURAL STEM CELLS. THE IDEA BEHIND THIS IS TO TREAT NEONATES THAT HAVE EXPERIENCED A HYPOXIC ISCHEMIC BRAIN INJURY EVENT. THE GOAL WOULD BE TO DEVELOP A PRODUCT FOR WHICH THEY COULD HAVE A PRE-IND MEETING AT THE END OF THIS AWARD.

SO IN TERMS OF SCORING, THIS ONE HAD AN 85. AND JUST, AGAIN, TO DISTINGUISH, THIS HAD A MEAN OF 84 AND HAD 11 GRANTS WORKING GROUP MEMBERS THAT VOTED IN FAVOR AND GAVE IT A SCORE THAT WAS IN THE FUNDABLE RANGE, FOUR THAT DID NOT.

WITH REGARDS TO 11544, SO THAT ONE IS ALSO USING FETAL-DERIVED NEURAL STEM CELLS. HERE IN TERMS OF PORTFOLIO, WE HAVE 17 PROJECTS IN SOLID TUMORS IN GENERAL. THERE ARE THREE THAT IN SOME WAY ADDRESS OVARIAN CANCER THAT ARE ALL VERY EARLY, SO DISCOVERY STAGE. ONE IS A PROJECT THAT IS LOOKING AT INTRODUCING RNAI THROUGH NANOPARTICLES AS A MECHANISM OF ADDRESSING DISEASE.

WE HAVE SOME CANDIDATE DISCOVERY, SO JUST TWO PROJECTS. ONE IS DEVELOPING AN IPSC-DERIVED NATURAL KILLER CELL IMMUNOTHERAPY AND A CAR-T CELL APPROACH. HOWEVER, THE CANDIDATE IN THIS PARTICULAR CASE USES AN APPROACH THAT'S PRETTY UNIQUE AMONG OUR PORTFOLIO. THAT IS THE ONCOLYTIC VIRAL THERAPY

COMBINED WITH CELLS THAT TARGET THE OVARIAN CANCER CELLS. SO THAT ITSELF CERTAINLY WOULD BE UNIQUE IN OUR PORTFOLIO.

CHAIRMAN THOMAS: WHAT WAS THE VOTE?

DR. SAMBRANO: AND THEN ON THAT ONE, THE SCORE THERE WAS A MEDIAN OF 85, THE MEAN IS 83, AND THERE WERE NINE MEMBERS THAT SCORED WITH A SCORE TO RECOMMEND AND SIX THAT SCORED BELOW.

MR. SHEEHY: ANY OTHER BOARD COMMENTS, QUESTIONS ABOUT THIS MOTION TO APPROVE THESE FOUR APPLICATIONS? IS THERE ANY PUBLIC COMMENT?

I JUST WANT TO PREFACE THIS. WE'RE GOING TO HOLD THIS OPEN. SO JUST TO PUT THAT OUT THERE.

DR. CHIU: I JUST WANTED TO RESPOND TO J.T.'S QUESTION. FIRST OF ALL, LET ME JUST SAY THAT YOU HAVE A NUMBER --

CHAIRMAN THOMAS: NAME?

MR. TORRES: YOU WANT TO INTRODUCE YOURSELF? WE ALL KNOW YOU.

DR. CHIU: ARLENE CHIU, FORMERLY FROM THE CITY OF HOPE. SO YOU HAVE AN ABUNDANCE OF 85S AND WE ARE SPLITTING HAIRS. AND I CERTAINLY UNDERSTAND HOW HARD IT IS TO COMPARE YOUR FAVORITE CHILD WITH YOUR OTHER FAVORITE CHILDREN. BUT WHAT I WANTED TO SAY IS THAT THIS 11544 DESERVES TO BE CONSIDERED AS

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PART OF THIS PACKAGE FOR THE FOLLOWING REASONS.

ONE, IT IS ALSO DERIVED FROM FETAL TISSUE-DERIVED NEURAL STEM CELLS WHICH HAVE A UNIQUE ABILITY TO HOME IN ON TUMOR CELLS. SO THIS PROJECT IS TO TARGET OVARIAN CANCER. AND AS DR. SAMBRANO HAS MENTIONED, YOU HAVE CURRENTLY, I THINK, THREE, IS IT, QUEST AWARDS FOR OVARIAN CANCER AND NOTHING MOVING DOWN THE PIPELINE.

IN CONTRAST, THIS ONE, THE PRODUCT ITSELF HAS GONE THROUGH FDA. YOUR EARLIER FUNDING OF THE APPLICANT HAS BROUGHT HER TO SEVERAL CLINICAL TRIALS USING THESE NEURAL STEM CELLS. NOW SHE'S PACKAGED THEM WITH A REALLY INNOVATIVE APPROACH OF USING ONCOLYTIC VIRUSES PACKAGED INTO THESE CELLS SO THAT THEY CAN TARGET THE TUMORS AND THEN LYSE AND REALLY WIPE THEM OUT. SO THIS IS UNIQUE.

THE SCIENCE OF ALL OF THESE ARE GREAT, AND I DON'T WANT TO COMPARE ONE SCIENCE PROJECT WITH ANOTHER. WHAT I DID WANT TO SAY IS ONE OF THE GOALS IS TO BRING A STEM CELL PRODUCT TO THE MARKET, A REAGENT OFF THE SHELF, UNLIKE AUTOLOGOUS-TYPE APPROACHES WHERE YOU HAVE TO DO THEM INDIVIDUALLY. ONE WOULD REALLY LIKE TO HAVE THESE CELLS THAT COULD BE USED IN MANY DIFFERENT INDICATIONS AND EASILY AVAILABLE. AND THIS POTENTIALLY COULD BE THAT. IT

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HAS ALREADY GONE THROUGH THE FDA FOR ONE INDICATION. SO IT'S ON A SHORT PATH TO GET THROUGH THE FDA FOR A DIFFERENT INDICATION, A VERY DESERVING INDICATION.

BUT NOT ONLY THAT, BECAUSE OF ALL THE STUDIES THAT HAVE GONE BEFORE, IF THIS WORKS, IT REALLY COULD IN SHORT ORDER BECOME ONE OF THESE REAGENTS THAT YOU CAN BUY OFF THE SHELF AND TREAT GLIOBLASTOMA IN ONE CASE, DEPENDING ON WHERE YOU PUT IT IN, OR INTO THE ABDOMEN AND TREAT OVARIAN CANCER.

SO FOR THAT REASON, AND ALSO FETAL STEM CELLS ARE NOT REALLY WELL RECEIVED BY THE NIH THESE DAYS, BUT I WOULD LIKE TO APPEAL TO YOU TO PUT THIS AMONGST YOUR OTHERS. BUT I DO HEAR MR. SHEEHY'S POINT, THAT THAT DOESN'T MEAN THIS WILL NOT GET FUNDED.

LAST, BUT NOT LEAST, THE PRICE TAG IS REALLY REASONABLE. THANK YOU.

MS. LANSING: CAN YOU HEAR ME?

MR. SHEEHY: YES.

MS. LANSING: CAN I SPEAK IN FAVOR --

MS. BONNEVILLE: NO, YOU CANNOT. THANK YOU.

MS. LANSING: I CAN'T SPEAK IN FAVOR OF THE OVARIAN CANCER ONE? I THOUGHT THAT WAS THE ONE I WASN'T CONFLICTED ON.

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MS. BONNEVILLE: NO. BECAUSE THERE ARE OPEN APPLICATIONS AND YOU'RE IN CONFLICT WITH SOME OF THEM, YOU CANNOT SPEAK TOWARDS THIS ONE.

MS. LANSING: SORRY.

MR. TORRES: MISS YOU.

MS. LANSING: I TRIED.

DR. ABOODY: HI. THANK YOU FOR LETTING ME SPEAK. I'M DR. KAREN ABOODY WITH CITY OF HOPE. I'M THE PI OF TRAN1-11544. YOU PREVIOUSLY FUNDED ME ON A DISEASE TEAM AWARD WHERE WE MET ALL THE MILESTONES AND GOT NIH FUNDING FOR THE CLINICAL TRIAL THAT'S ONGOING.

IN RESPONSE, THERE ARE 22,000 WOMEN PER YEAR IN THE U.S. AFFLICTED WITH OVARIAN CANCER. IT IS THE MOST LETHAL GYNECOLOGICAL MALIGNANCY WITH AN EXCEPTIONALLY HIGH MORTALITY RATE LARGELY BECAUSE THE MAJORITY OF THE PATIENTS PRESENT AT ADVANCED STAGE, STAGE 3 WITH ABDOMINAL METASTASIS, WHICH IS WHAT WE ARE TARGETING. THE MEDIAN SURVIVAL FOR THESE PATIENTS IS LESS THAN THREE YEARS FOLLOWING STANDARD-OF-CARE SURGERY AND CHEMO. A LOT OF THESE WOMEN CANNOT FINISH THE CHEMO REGIMEN BECAUSE THE CHEMO IS SO TOXIC THAT THEY HAVE NAUSEA, ABDOMINAL PAIN, AND VOMITING. SO THEY'RE NOT EVEN ABLE TO FINISH THE CHEMO.

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FURTHERMORE, THEY DEVELOP CHEMO RESISTANCE. THIS IS CISPLATIN PACLITAXEL.

OKAY. THE CURRENT THERAPIES CANNOT HELP THESE WOMEN. THERE'S AN URGENT NEED FOR A MORE EFFECTIVE TARGETED THERAPY THAT CAN ALSO IMPROVE QUALITY OF LIFE DURING TREATMENT, WHICH IS AS IMPORTANT AS IMPROVING CRITICAL OUTCOMES IN MY MIND. THIS TUMOR-KILLING ONCOLYTIC VIRAL THERAPY CAN KILL CHEMO-RESISTANT AND RADIO-RESISTANT CELLS. IT LYSES THE CELLS. IT RELEASES MORE VIRAL PARTICLES, AND IT HAS AN AMPLIFYING EFFECT. SO IF YOU CAN SEED THE VIRUS IN EACH OF THOSE METASTATIC TUMOR SITES, IT SHOULD KEEP GOING TILL IT IS NORMAL TISSUE AND IT WILL STOP.

THERE ARE CURRENTLY SOME CLINICAL TRIALS WHERE THEY'RE PUTTING FREE ONCOLYTIC VIRUS INTO THE PATIENT. OKAY. IT HAS DEMONSTRATED SAFETY. THEY'RE DISAPPOINTED IN THE UPTAKE BECAUSE THEY'RE NOT GETTING THE VIRUS TO THE TUMOR SITES. THE VIRUS IS GETTING ELIMINATED BY THE PATIENT'S IMMUNE SYSTEM BEFORE IT EVEN GETS TO THE TUMOR. WHEN IT DOES GET TO THE TUMOR, IT'S NOT GETTING DISTRIBUTED IN THE METASTASIS. THE STEM CELLS, NOW WE HAVE DATA, THEY ARE TARGETING, THEY'RE DELIVERING THE VIRUS TO THE OVARIAN METASTASIS IN OUR ANIMAL MODELS. THEY'RE

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PROTECTING IT FROM THE IMMUNE SYSTEM IN IMMUNOCOMPETENT ANIMALS. WE KNOW PATIENTS CAN GET MULTIPLE TREATMENT ROUNDS OF THESE NEURAL STEM CELLS WITHOUT REJECTING THEM IMMUNOLOGICALLY. THEY'RE NOT -- THEY'RE HLA CLASS II NEGATIVE.

WE HAVE THE MANUFACTURING PROCESS READY. WE HAVE GMP VIRUS. WE ARE IN CLINICAL TRIAL FOR BRAIN TUMOR PATIENTS NEWLY DIAGNOSED. THE FIRST EIGHT PATIENTS HAVE DEMONSTRATED SAFETY USING THE EXACT SAME PRODUCT. OUR STEM CELLS MAKE A RISK-FREE VIRUS. I CAN TAKE IT TO THE CLINIC VERY QUICKLY. WE HAVE OUR CLINICIANS EXCITED ABOUT IT. WE HAVE THE TEMPLATE, WE HAVE THE TEAM, WE KNOW HOW TO GET IT INTO THE CLINIC, AND HAVE THE PRE-IND MEETING PROBABLY BEFORE THE END OF THE TERM. OUR (UNINTELLIGIBLE) SPECIFICALLY LOWERED TO THE TYPES THAT WE NEED TO GET IT THERE. AND THERE IS URGENCY IN MY MIND, AND THE CLINICIANS REALLY WANT THIS TO MOVE FORWARD NOW. THEY DON'T HAVE ANYTHING TO TREAT THESE PATIENTS WITH. THANK YOU.

MR. SHEEHY: OTHER PUBLIC COMMENT? I THINK YOU WERE FIRST AND THEN DR. SNIDER, I BELIEVE. I MISSED SOMEBODY BACK THERE. ONE, TWO, THREE, FOUR. OKAY.

DR. CHEN: GOOD MORNING. THANK YOU ALL

FOR THE OPPORTUNITY TO SPEAK. I'M ACTUALLY GOING TO ADVOCATE FOR 11555, AND THE REASON IS I THINK IF THIS MOTION PASSES --

MR. TORRES: STATE YOUR NAME FOR THE RECORD PLEASE.

DR. CHEN: SORRY. MY NAME IS YVONNE CHEN, FACULTY FROM UCLA, THE PI FOR TRAN1-11555. AND SO I CERTAINLY UNDERSTAND OUR WISH TO PROMOTE RESEARCH; AND AS ONE OF THE BOARD MEMBERS MENTIONED, I THINK IT'S IMPORTANT TO CONSIDER THE DISEASE TYPE AND THE UNMET NEED THAT EXISTS.

OUR APPLICATION FOCUSES ON SUBMITTING AND GETTING APPROVAL FOR AN IND FOR A PHASE 1 CLINICAL TRIAL TO TREAT MULTIPLE MYELOMA. MULTIPLE MYELOMA IS AN INCURABLE DISEASE. IT AFFECTS 32,000 NEW PATIENTS EVERY YEAR. AT UCLA WE TREAT OVER A THOUSAND EVERY YEAR JUST AT UCLA. AND THIS BEING AN INCURABLE DISEASE, WE HAVE FAR MORE PATIENTS WHO WISH TO GO ON CLINICAL TRIALS THAN WE HAVE SPACE FOR. AND SO THIS IS A TRULY UNMET NEED, AND WE HAVE DEVELOPED A NOVEL TECHNOLOGY THAT SIMULTANEOUSLY TARGETS TWO ANTIGENS PRESENT ON MULTIPLE MYELOMA CELLS THAT CAN HELP US INCREASE DURABILITY OF RESPONSE, WHICH IS CURRENTLY THE GREATEST CHALLENGE IN THE TREATMENT OF MULTIPLE MYELOMA.

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I WOULD LIKE TO ALSO MENTION THAT OUR TEAM HAS PERFORMED EXTENSIVE PRECLINICAL TESTING AND HAS MOVED THIS PROJECT ALONG VERY QUICKLY. WITHIN THE PAST FOUR MONTHS SINCE WE -- OR THREE MONTHS SINCE WE SUBMITTED THIS APPLICATION, WE'VE ALREADY MADE SIGNIFICANT PROGRESS. NO. 1, WE GAINED FDA APPROVAL FOR ANOTHER IND ON THE BISPECIFIC T-CELL THERAPY THAT MY GROUP HAS DEVELOPED DEMONSTRATING THAT WE ARE ABLE TO ACTUALLY EXECUTE CLINICAL MANUFACTURING AND PROVIDE SUCCESSFUL IND PREPARATION FOR CAR-T CELL THERAPY.

AND NO. 2, WE HAVE SUBSEQUENTLY PERFORMED ADDITIONAL MOUSE IN VIVO STUDIES DEMONSTRATING VERY STRONG EFFICACY USING OUR T-CELLS IN THE TREATMENT OF ADVANCED, AGGRESSIVE MULTIPLE MYELOMA.

AND SO I WOULD LIKE TO URGE THE BOARD AND THE COMMITTEE MEMBERS TO CONSIDER BASED ON THE TRUE EXISTING UNMET NEED OF THIS INCURABLE DISEASE THAT AFFLICTS SO MANY PEOPLE AND ALL OF THEM INVARIABLY RELAPSE AFTER MULTIPLE LINES OF TREATMENT TYPICALLY IN THE TIME FRAME OF FIVE TO TEN YEARS. AND THIS IS REALLY A NOVEL TECHNOLOGY USING CELL TYPES THAT CIRM HAS REPEATEDLY SUPPORTED JUST THIS MORNING WITH ANOTHER CLIN2 GRANT THAT I THINK SHOWS REAL PROMISE IN CURING A TERRIBLE DISEASE. THANK YOU.

MR. TORRES: I WANTED TO ADD A COMMENT, NOT TO YOUR PROPOSAL. I WAS REMISS IN NOT THANKING DR. ABOODY WHO I HAD FIRST MET WHEN I FIRST CAME ON THIS BOARD AND HAVE MARVELED AT HER RESEARCH ESPECIALLY WITH BRAIN TUMORS.

AND I WAS THE PATIENT ADVOCATE REVIEWER ON YOUR GRANT BECAUSE I KNOW HOW IMPORTANT JEFF FEELS ABOUT OVARIAN CANCER GIVEN HIS FAMILIAL HISTORY. AND I ESPECIALLY, BECAUSE, AS SHERRY WELL KNOWS AND SO SHE CANNOT SPEAK ON THIS, BUT I CAN, IT'S A TREMENDOUS UNMET NEED AND SOMETHING THAT WE HAVE NOT DONE FOR WOMEN IN THIS STATE. AND SO I JUST WANT TO THANK YOU AGAIN, AND I KNOW IT'S GOING TO CONTINUE TO BE OPEN, RIGHT, AS WE MOVE FORWARD. BUT THANK YOU, KAREN.

DR. MARTIN: I HAVE ANOTHER QUESTION RELEVANT TO AN EARLIER ONE, AND THAT IS IN THE CLINICALTRIALS.GOV, HOW MANY CAR-T TRIALS ARE ONGOING THAT ARE TARGETING MULTIPLE MYELOMA?

MR. SHEEHY: PERHAPS WE COULD HAVE SOMEBODY RESEARCH THAT FOR A MINUTE, BUT WE ARE IN PUBLIC COMMENT RIGHT NOW, AND WE HAVE DR. SNIDER COMING UP. WE CAN BRING THE APPLICANT. I THINK SHE KNOWS THE ANSWER. WE WILL BRING HER UP AFTER DR. -- WELL, IF YOU CAN GIVE A QUICK ANSWER.

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DR. CHEN: SO I CAN COMMENT. SO THERE ARE MULTIPLE CLINICAL TRIALS -- THERE ARE MULTIPLE CLINICAL TRIALS TARGETING MULTIPLE MYELOMA USING CAR-T CELLS AND NONE THAT ACTUALLY HAS LYSE SPECIFICITY. IN ALL OF THE TRIALS THAT HAVE REPORTED SO FAR HAVE SHOWN POOR PERSISTENCE IN LARGE PART DUE TO ANTIGEN LOSS. AND THAT'S PRECISELY THE CHALLENGE THAT WE ARE TRYING TO ADDRESS AND HAVE SHOWN CLINICAL EFFICACY TO ADDRESS BY USING A BISPECIFIC CAR-T CELL.

MR. SHEEHY: THANK YOU. INTRODUCE YOURSELF, DR. SNYDER.

DR. SNYDER: YEAH. HI. MY NAME IS EVAN SNYDER. I'M THE PI ON 628. I DID SUBMIT A LETTER LAST WEEK THAT GOES INTO MUCH MORE DETAIL ABOUT OUR MOTIVATION AND RATIONALE.

AND I'M THE ONLY ONE SPEAKING HERE ON BEHALF OF THE KIDS. IT'S TAKEN ME 25 YEARS TO GET HERE IN FRONT OF YOU TO BE ABLE TO BE ON THE THRESHOLD OF DOING SOMETHING FOR KIDS WITH PERINATAL ASPHYXIA, THAT IF NOTHING IS DONE WILL GO ON TO DEVELOP CP.

MR. SHEEHY: COULD YOU PLEASE --

DR. SNYDER: GO ON TO DEVELOP CEREBRAL PALSY. IT IS COMMON, DESTABLING, AND IN IMPACT, NOT

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JUST THE KIDS, FOR DECADES, BUT THEIR FAMILIES AND SOCIETY.

AS A STEM CELL BIOLOGIST, AS A NEONATOLOGIST, AS A PEDIATRIC NEUROLOGIST, I'M ABSOLUTELY PASSIONATE ABOUT THIS. I KNOW THE DISEASE, I KNOW THE KIDS, I KNOW WHAT HAPPENS TO THE BABIES IF YOU DON'T DO SOMETHING ABOUT IT. I KNOW EVERY ASPECT OF HOW THIS INTERVENTION THAT WE TALKED ABOUT CAN BE PIGGYBACKED UPON THE ROUTINE NEONATAL CARE OF THESE KIDS, INCLUDING THE IMAGING, THE PATIENT SELECTION, THE ADMINISTRATION OF THE CELLS, WHICH WILL NOT ALTER THE COURSE, BUT WILL ALTER THEIR OUTCOME.

I THINK IT WAS MENTIONED BY GIL. CIRM HAS NO -- HAS VERY FEW PEDIATRIC NEUROLOGY INDICATIONS IN THE PORTFOLIO AND NONE FOR BABIES. ON THE OTHER HAND, IF YOU ACCEPT THAT STEM CELL BIOLOGY IS PART OF DEVELOPMENTAL BIOLOGY AND THE IMMATURE NEONATAL BRAIN IS IN THE MIDST OF ACTIVE PLASTICITY AND DEVELOPMENT, THERE IS NO GREATER OPPORTUNITY TO HAVE AN IMPACT OF THIS BIOLOGY ON KIDS THAT NEED THIS.

I'VE ALSO TAKEN CARE OF THE KIDS WHEN NOTHING HAS HAPPENED, AND THERE IS NOTHING OUT THERE. WE CAN MAKE AN IMPACT FOR DECADES. THE RATIONALE IS SOLID. THERE IS AN AREA THAT CAN BE

IMAGED CALLED THE PENUMBRA AROUND THE INJURY. THIS IMAGING CORRELATES WITH THE MOLECULAR PROFILE THAT WILL RESPOND TO THE KNOWN MECHANISM OF ACTION OF THE CELLS. THESE KIDS CAN BE SELECTED, THEY CAN BE ADMINISTERED THE CELLS, AND I THINK THERE'S AN ENORMOUSLY HIGH LIKELIHOOD OF A SUCCESSFUL CLINICAL TRIAL.

THE TWELVE NICUS IN SOUTHERN CALIFORNIA ARE IN PLACE AND READY TO LAUNCH. THIS, IN FACT, WOULD ACTUALLY BE THE FIRST BIOMARKER FOR REGENERATIVE MEDICINE THAT ACTUALLY RATIONALLY CHOOSES PATIENTS BASED ON THE MECHANISM OF ACTION OF THE STEM CELLS. SO IT'S INFORMATIVE NOT JUST FOR THESE KIDS, BUT FOR THE ENTIRE FIELD.

THE LAST THING I'LL SAY, IF WE DON'T GET INVOLVED, I'M AFRAID THE CHARLATANS THAT ARE ALREADY APPROACHING THESE PARENTS WITH CEREBRAL PALSY WILL FILL THE BRIDGE.

MR. SHEEHY: THANK YOU, DR. SNYDER. SO NEXT WE HAVE TWO FOLKS OVER HERE, THREE. IF YOU ARE COMFORTABLE, WE CAN MOVE DOWN THE ROW. PLEASE.

DR. KUO: MY NAME IS CAROLINE KUO. I'M AN IMMUNOLOGIST AT UCLA, AND I'M THE PI OF THE TOP GRANT, 11536. WE HAVE BEEN WORKING ON THIS PROJECT FOR THE LAST SEVEN YEARS. AND WE CURRENTLY HOLD A

DISC AWARD THAT HAS HELPED IDENTIFY THE REAGENTS THAT WE WILL BE USING FOR THIS TRAN AWARD.

AND SO FIRST OFF, I'D LIKE TO SAY THAT I THINK THAT THIS PROJECT IS CONSISTENT WITH THE CIRM MISSION IN THAT WE ARE USING HUMAN HEMATOPOIETIC STEM CELLS THAT ARE GENE MODIFIED. AND TO ECHO DR. JUELSGAARD, THIS TREATMENT IS INTENDED FOR A POPULATION THAT IS IN DESPERATE NEED OF NEW THERAPEUTIC OPTIONS.

SO THE CURRENT SURVIVAL RATE FOR X-LINKED HYPER IGM IS 25 PERCENT AT 25 YEARS OF AGE. AND SO ALL THE CURRENT THERAPIES THAT ARE AVAILABLE ARE REALLY VERY TEMPORARY AND CANNOT BE CURATIVE AND STILL ALLOWS THE DISEASE TO PROGRESS.

AND SO WE HAVE REALLY STRUCTURED THIS APPLICATION AROUND A PRE-IND MEETING THAT WE HAD, PRE, PRE-IND MEETING THAT WE HAD WITH THE FDA IN FEBRUARY. AND SO WE FEEL THAT WE HAVE FILLED A NEED AND A VERY CLEAR SET OF MILESTONES THAT CAN BE COMPLETED QUICKLY AND IN A REASONABLE FASHION.

I'LL ALSO ADD THAT MY SCIENTIFIC MENTOR IS DR. DONALD KOHN, AND MY LAB IS ADJACENT TO HIS LAB. AND SO WE'VE ESTABLISHED A VERY SYNERGISTIC RELATIONSHIP, AND SO THIS PROJECT CAN REALLY TAKE ADVANTAGE OF THE SUCCESS THAT HE'S HAD WITH GENE

THERAPY FROM A CLINICAL PERSPECTIVE AND REALISTICALLY BRING THIS PROJECT TO THE CLINIC. THANK YOU VERY MUCH.

MR. SHEEHY: THANK YOU. NEXT COMMENTER.

DR. TUSZYNSKI: GOOD AFTERNOON. I'M MARK TUSZYNSKI. I'M A PHYSICIAN SCIENTIST AT THE UNIVERSITY OF CALIFORNIA SAN DIEGO AND THE DIRECTOR OF THE UCSD TRANSLATIONAL NEUROSCIENCE INSTITUTE, AND I'M SPEAKING ON APPLICATION 11579 ON BEHALF OF MY CO-APPLICANT.

I'M GRATEFUL FOR THE OPPORTUNITY TO RELAY A FEW POINTS RELATED TO THE CONSIDERATION OF OUR PROPOSAL. SO, FIRST, WITH REGARD TO PROGRAMMATIC IMPACT, WE ARE THE ONLY STEM CELL PROJECT IN THE CIRM PORTFOLIO THAT AIMS TO TREAT SEVERE SPINAL CORD INJURY. SO WE AIM TO RECONNECT DAMAGED CONNECTIONS IN THE SPINAL CORD, ADDRESSING A GREAT UNMET MEDICAL NEED THAT CURRENTLY HAS NO TREATMENT.

OTHER SCI-, SPINAL CORD INJURY, RELATED, PROJECTS IN CIRM'S PORTFOLIO TARGET THE RELATIVELY SMALL POPULATION OF UNINJURED CONNECTIONS IN AN EFFORT TO PROMOTE REINSULATION OF THE WIRES, THE AXONS THAT ARE IN THE INJURY SITE, AND THAT MAY HAVE A RELATIVELY MINOR IMPACT ON PATIENTS WITH SEVERE INJURY WHO HAVE LOST THE CONNECTIONS.

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OUR PROGRAM SIGNIFICANTLY WIDENS THE POTENTIAL SCOPE AND THE IMPACT OF CIRM FUNDING BY TRYING TO FORM NEW CONNECTIONS IN SEVERELY INJURED PATIENTS. AND THIS PROGRAM IS BASED ON BIOLOGY THAT IS ASTONISHING IN COMING BACK TO YOUR COMMENT ABOUT THE VALUE OF NEURAL STEM CELLS OR STEM CELLS GENERALLY. HUNDREDS OF THOUSANDS OF AXONS EMERGE FROM STEM CELLS, SO CAN ACTUALLY EMERGE FROM STEM CELL GRAFTS PLACED IN AN INJURY SITE AND TRAVEL BELOW.

SECONDLY, WITH REGARD TO PATIENT IMPACT, THIS PROGRAM HAS BEEN SUPPORTED BY CIRM FROM ITS EARLIEST STAGES OF DEVELOPMENT TO THE PRESENT LEVEL OF TRANSLATIONAL READINESS. AND UPON COMPLETING THE WORK IN THIS TRAN GRANT, WE WILL BE READY TO INITIATE HUMAN CLINICAL TRIALS IN SEVERE SPINAL CORD INJURY. SO THE INTENT OF THIS GRANT IS TO FUND THE PRODUCTION OF OUR CLINICAL TRIAL CELL LINE AND ESTABLISH STANDARDS FOR THE TESTING AND RELEASE OF THESE CELLS TO PATIENTS AND THEIR PHYSICIANS. AND, OF COURSE, WE HOPE TO COMPLETE THIS PROGRAM WITH FUNDING UNDER THIS TRAN GRANT.

I'D ALSO LIKE TO SAY THAT WE HAVE EVIDENCE OF EFFECTIVENESS IN PRIMATES. SO WE HAVE SHOWN THE EFFECTIVENESS OF THE STEM CELL THERAPY IN SPINAL

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CORD INJURY MODELS IN SEVERAL RAT EXPERIMENTS, AND WE NOW HAVE PUBLISHED DATA OF EFFICACY IN NONHUMAN PRIMATES WITH SPINAL CORD INJURY. SO OUR DEMONSTRATION OF EFFECTIVENESS IN MONKEYS IS UNIQUE, TO OUR KNOWLEDGE, AMONG STEM CELL PROGRAMS FOR NEUROLOGICAL DISEASE, IN PARTICULAR SPINAL CORD INJURY, AND STRONGLY SUPPORTS BRINGING THIS PROGRAM TO PATIENTS.

AND FINALLY, I'D LIKE TO COMMENT ON THE STRENGTH OF THE SCIENCE AND THE EXPERIENCE OF OUR RESEARCH TEAM. SO WE HAVE PUBLISHED RESULTS FROM THIS PROGRAM IN THE TOP JOURNALS IN SCIENCE INCLUDING SIX PAPERS IN TOP NATURE JOURNALS IN THE RECENT YEARS, SUPPORTING THE QUALITY AND DEPTH OF OUR PROGRAM. AND WE HAVE A TEAM OF PHYSICIANS READY TO LINE THIS UP FOR CLINICAL TRIAL. SO WE ARE GRATEFUL FOR THE SUPPORT WE HAVE HAD AND HOPE WE CAN MOVE FORWARD. THANK YOU.

CHAIRMAN THOMAS: MR. CHAIRMAN, CAN I ASK A QUESTION OF THE PI?

TO THE EXTENT THAT THE PRODUCT ULTIMATELY PROVES TO BE EFFICACIOUS, OBVIOUSLY ONE OF THE BIG QUESTIONS IN SPINAL CORD INJURY IS WHAT'S THE WINDOW POSTINJURY IN WHICH SOMETHING MIGHT BE EFFECTIVE? WHAT IS YOUR HYPOTHESIS AS FAR AS THAT GOES? IS

THAT SOMETHING YOU CAN'T REALLY SAY UNTIL YOU GET INTO THE CLINICAL TRIAL PROCESS?

DR. TUSZYNSKI: NO. NO. SO WE HAVE PRELIMINARY INDICATION FROM THE ANIMAL EXPERIMENTS. SO WE SEE EFFICACY FROM A TWO-WEEK WINDOW TO A THREE-MONTH WINDOW. AND WE ARE CURRENTLY DOING ONGOING STUDIES IN CHRONIC INJURY IMPLANTING CELLS ONE YEAR AFTER THE INJURY IN MONKEYS. SO FOR CHRONIC INJURY, IT'S ONGOING WORK, BUT WE HAVE EVIDENCE FOR THIS WINDOW OF TWO WEEKS TO THREE MONTHS AFTER.

CHAIRMAN THOMAS: THANK YOU.

MR. TORRES: RHESUS MONKEYS?

DR. TUSZYNSKI: YES.

MR. SHEEHY: THANK YOU, DOCTOR. NEXT. I KNOW JEANNE. WE HAVE SOMEONE ELSE, BUT YOU CAN FOLLOW.

DR. GARBAZEF: HI. I WANT TO THANK THE BOARD FOR GIVING ME AN OPPORTUNITY TO SPEAK. I'M A POST-DOC IN THE (UNINTELLIGIBLE), AND I'LL BE TALKING ON BEHALF OF PROJECT 11579. SO, HELLO. MY NAME IS HELENA GARBAZEF (PHONETIC).

ABOUT THREE YEARS AGO, WHILE IN GRADUATE SCHOOL AT STANFORD UNIVERSITY, I FELL IN A ROCK CLIMBING ACCIDENT IN YOSEMITE NATIONAL PARK. I WAS

AIRLIFTED TO STANFORD HOSPITAL AND UNDERWENT EMERGENCY SURGERY FOR MY FALL. I HAVE AN L1 SPINAL CORD INJURY. I RETURNED TO GRADUATE SCHOOL AFTER MY ACCIDENT. AFTER I FINISHED MY DEGREE, I JOINED THE TUSZYNSKI LAB BECAUSE OF THE PROMISE OF NEURAL STEM CELL THERAPY FOR SPINAL CORD INJURY.

THIS APPROACH ALLOWS US TO REPLACE NEURAL TISSUE LOST TO TRAUMA. THE GRAFT STEM CELLS PROMOTE THE GROWTH OF INJURED NEURONS. THEY MATURE TO BECOME FUNCTIONAL NEURONS AND CONNECT TO CELLS ABOVE AND BELOW THE LESION SITE. THEY CREATE A RELAY THAT ALLOWS THE BRAIN TO TALK TO THE SPINAL CORD AGAIN.

WE'VE TAKEN THIS APPROACH FROM RATS TO GRAFTING HUMAN EMBRYONIC STEM CELLS INTO NONHUMAN PRIMATES TO SHOW SAFETY AND EFFICACY AT EVERY STEP. THERE'S CURRENTLY NO TREATMENT FOR SPINAL CORD INJURY. THESE INJURIES HAPPEN TO YOUNG PEOPLE. THEY ARE A LIFE SENTENCE OF SEVERE AND OFTEN COMPLETE LIMITATION, OF DEBILITATING PAIN, DEPENDENCE ON CAREGIVERS, AND LOSS OF OUR MOST BASIC FUNCTIONS.

MY INJURY COMPLETELY DISRUPTED MY LIFE, AND I'M A MILD AND LUCKY CASE. I'VE MET MANY YOUNG PEOPLE IN WHEELCHAIRS THROUGH MY INVOLVEMENT WITH THE ADAPTIVE SPORTS COMMUNITY AND THROUGH PATIENT

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ADVOCACY THROUGH SCIENCE, EDUCATION, AND OUTREACH. I THINK ABOUT THEM EVERY DAY AS I WORK IN THE LAB. I'M HERE BOTH AS A SCIENTIST AND AS A PATIENT ADVOCATE.

WE NEED AN INTERVENTION FOR SPINAL CORD INJURY THAT HAS THE POTENTIAL TO TREAT ALL THE EFFECTS OF DAMAGE TO THE CENTRAL NERVOUS SYSTEM. THIS INJURY AFFECTS MANY FUNCTIONS, AND THE NEURAL STEM CELL GRAFT IS AN OPPORTUNITY TO RESTORE SO MUCH MORE THAN JUST STEPPING.

I WANT TO END BY THANKING CIRM FOR ALL THE WORK THAT YOU'VE DONE SO FAR. EVEN BEFORE IN MY CURRENT POSITION, AS A STUDENT AT STANFORD WORKING IN A STEM CELL LAB, I SAW FIRSTHAND THE IMPACT FUNDING FROM CIRM HAS ON EXCITING FLEDGLING WORK AND HOW SUPPORT FROM THIS ORGANIZATION STIMULATED AND ENERGIZED MY FIELD. SO THANK YOU.

MR. TORRES: I JUST WANT TO SAY WHAT A PLEASURE IT WAS TO MEET YOU EARLIER BECAUSE I ESCORTED YOU THROUGH SECURITY. I'M READING ALL YOUR WHOLE HISTORY, BUT NOW THAT I DO, I LOVE YOU EVEN MORE. SO THANK YOU. WE'RE HONORED BY YOUR PRESENCE.

MR. SHEEHY: THANK YOU. DR. LORING.

DR. LORING: MY NAME IS JEANNE LORING, AND

I AM FROM THE SCRIPPS RESEARCH INSTITUTE AND ASPEN NEUROSCIENCE, A NEW START-UP COMPANY. BUT I AM A COLLABORATOR ON 11548, THE TRAUMATIC BRAIN INJURY GRANT. THE PI IS BRIAN CUMMINGS AT UCI, BUT I AM NOT HERE AS A COLLABORATOR, I'M HERE AS A SURROGATE FOR DON REED, WHO YOU ALL KNOW. DON HAS ASKED ME TO READ HIS LETTER, AND IT IS A TREMENDOUS HONOR KNOWING HOW MUCH DON HAS DONE FOR CIRM OVER ALL THESE YEARS, AND I'M EXTREMELY HAPPY TO STAND IN FOR HIM.

"WILL THERE BE A PROP 71 PART 2? THAT DECISION IS NOT MINE TO MAKE. BUT I ABSOLUTELY KNOW WHAT I DO WANT, AND THAT IS A MAJOR RENEWAL OF FUNDING. THE BEST WAY TO MOVE TOWARD THAT GOAL, I BELIEVE, IS TO TAKE ON A TRULY HUGE PROBLEM -- AND THEY JUST DON'T GET ANY BIGGER THAN TRAUMATIC BRAIN INJURY. EVERY YEAR, MORE THAN 200,000 CALIFORNIANS RECEIVE A TRAUMATIC BRAIN INJURY, AT A FINANCIAL COST OF ROUGHLY 9.6 BILLION, AN AMOUNT MORE THAN THREE TIMES CALIFORNIA'S ENTIRE TEN-YEAR INVESTMENT IN CIRM. ACROSS OUR COUNTRY, 1.7 MILLION CITIZENS SUFFER A TBI – AT THE STAGGERING EXPENSE OF $76.5 BILLION. MORE PEOPLE HAVE A TRAUMATIC BRAIN INJURY THAN ARE AFFECTED BY CANCERS OF THE BRAIN, BREAST, COLON, LUNG AND PROSTATE PUT TOGETHER.

"WHAT IS IT LIKE TO HAVE A TRAUMATIC BRAIN INJURY? OFTEN COMPARED TO ALZHEIMER'S DISEASE, TBI DESTROYS MEMORY AND BRINGS EMOTIONAL CONFUSION TO THE SUFFERER. WHILE TBI AFFECTS SIMILAR NUMBERS OF CALIFORNIANS WITH ALZHEIMER'S DISEASE, TBI IS MUCH LESS KNOWN AND MIGHT BE CALLED A SILENT EPIDEMIC.

THE PRIMARY INVESTIGATOR FOR THIS PROJECT, BRIAN CUMMINGS, TOLD ME OF A FAMILY SUMMER CAMP FOR CHILDREN TO WHICH HE BROUGHT HIS DAUGHTER. WHILE THERE, HE MET A WOMAN WHO HAD BEEN A SOLDIER IN THE IRAQ WAR WHERE SHE TWICE RECEIVED TBIS FROM ONE OF THOSE GHASTLY HOME-MADE BOMBS, AN IED. WHAT BROUGHT THE MEANING OF THE TRAUMATIC BRAIN INJURY HOME TO DR. CUMMINGS WAS THAT THIS WOMAN SOLDIER COULD NOT REMEMBER WHICH CHILD WERE HER CHILDREN.

"TBI, AT PRESENT, IS INCURABLE. AS YOU KNOW, FOR MORE THAN 25 YEARS I HAVE BEEN SUPPORTING RESEARCH FOR THE RELATED CONDITION OF SPINAL CORD INJURY. AND FOUR OF OUR GREATEST RESEARCH CHAMPIONS ARE AILEEN ANDERSON, HANS KEIRSTEAD, GABRIEL NISTOR, AND BRIAN CUMMINGS. ALL FOUR OF THESE OUTSTANDING SPINAL CORD INJURY SCIENTISTS -- THIS TIME LED BY BRIAN CUMMINGS AS THE TBI EXPERT -- WILL BE INVOLVED IN THIS PROJECT. THEIR GOAL? "TRANSPLANTATION OF HUMAN NEURAL STEM CELLS COULD LEAD TO IMPROVEMENTS

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IN LEARNING, MEMORY AND EMOTION (TO) SIGNIFICANTLY CHANGE A PATIENT'S --

"IN ADDITION, FOUR YOUNG SCIENTISTS FROM CIRM'S BRIDGES PROGRAM WILL BRING THE ENERGY AND PASSION OF YOUTH TO THIS ENDEAVOR. THIS IS CIRM AT ITS VERY BEST. I URGE YOUR SUPPORT."

AND I SUPPOSE YOU DON'T KNOW, DON REED IS VICE PRESIDENT FOR PUBLIC POLICY FOR AMERICANS FOR CURES. I KNOW I'M NOT AS GOOD AS HE IS.

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

MR. PEREZ: MY NAME IS VICTOR PEREZ. I AM A MEDICAL SOCIAL WORKER AT THE REHABILITATION INSTITUTE OF SOUTHERN CALIFORNIA, ALSO KNOWN AS RIO, AND I'M HERE TO ADVOCATE ON BEHALF OF BRIAN CUMMINGS' PROJECT, TRAN1-11548.

SO AT RIO WE HAVE BEEN SUPPORTING CALIFORNIA RESIDENTS WHO HAVE SUFFERED A TRAUMATIC BRAIN INJURY SINCE 1950. I HAVE WORKED FOR RIO FOR ABOUT TWO YEARS NOW PRIMARILY AS A COUNSELOR, AS A SOCIAL WORKER, AND MOST OF OUR TBI PATIENTS WHO ARE PARTICIPANTS THERE ARE CONSIDERED WITH HIGH ACUITY AND REQUIRE SIGNIFICANT ASSISTANCE WITH ACTIVITIES OF DAILY LIVING AS WELL AS 24-HOUR SUPERVISION.

PEOPLE WITH MODERATE TO SEVERE TBI

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TYPICALLY VARY IN CHRONIC HEALTH PROBLEMS CONSIDERING THAT 57 PERCENT OF THEM ARE MODERATELY OR SEVERELY DISABLED, 55 PERCENT OF THEM DO NOT HAVE A JOB, BUT AT THE TIME OF INJURY DID. FIFTY PERCENT OF THEM RETURNED TO A HOSPITAL AT LEAST ONCE, AND 33 PERCENT OF THEM RELY ON HELP FOR EVERYDAY ACTIVITIES. TBI SURVIVORS OFTEN EXPERIENCE A LOSS OF INDEPENDENCE, OFTENTIMES THROUGH THE COMPLICATION OF APHASIA.

UNFORTUNATELY, I HAVE WITNESSED THE STRUGGLE AS I OBSERVE MANY OF THE PARTICIPANTS I COUNSEL. I CAN ONLY RELATE TO THIS PHENOMENON OF LETHOLOGICA, OR THE EXPERIENCE OF THE TIP OF THE TONGUE WHERE YOU WANT TO SAY THE WORD, BUT YOU JUST CAN'T QUITE REMEMBER IT. SO IMAGINE THAT ON AN ONGOING BASIS, NOT BEING ABLE TO QUITE GET THAT WORD OUT. I CAN.

I CAN ALSO TELL YOU THAT TBI'S ARE QUITE EMOTIONAL FOR THESE INDIVIDUALS, OFTENTIMES SUFFERING FROM ANXIETY, ANGER, FRUSTRATION, CONFUSION, AND EVEN SOMETIMES DEPRESSION.

SO NOW I WANT YOU TO IMAGINE BRIAN, A 15-YEAR-OLD YOUNG MAN AS HE'S EXPERIENCING THE LIVELIHOOD OF BEING A TEENAGER LEARNING HOW TO RIDE A SKATEBOARD. UNBEKNOWNST TO BRIAN, HIS LIFE WOULD

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FOREVER CHANGE AS HE IS HIT BY A CAR.

HAVING KNOWN WHAT IT WAS LIKE TO LIVE A FAIRLY INDEPENDENT LIFE, HE NOW MUST LEARN TO RELIVE WHAT IT'S LIKE TO BE BRIAN. EVENTUALLY BRIAN WOULD GROW TO LOSE INTEREST IN DAILY ACTIVITIES AND DEVELOP DEPRESSION. FORTUNATELY, BRIAN HAS TWO LOVING PARENTS WHO HAVE ADVOCATED FOR HIM TO BE ENROLLED IN A PROGRAM AT RIO TO HAVE HIS NEEDS MET, INCLUDING ADDRESSING THAT EMOTIONAL DISTRESS. IF A CELL THERAPY COULD PARTIALLY IMPROVE BRIAN'S ABILITIES, HIS LIFE WOULD BE GREATLY IMPROVED.

ON BEHALF OF THE REHABILITATION INSTITUTE OF SOUTHERN CALIFORNIA, MY COLLEAGUES, AND THE PARTICIPANTS THAT I SERVE, THEY HAVE SENT ME HERE TO ENTHUSIASTICALLY ENDORSE DR. CUMMINGS' PROJECT BASED AT UC IRVINE WITH AIMS TO ESTABLISH SAFETY AND EFFICACY OF HUMAN NEURAL STEM CELLS AS THERAPY FOR TBI. IF SUCCESSFUL, DR. CUMMINGS' WORK COULD ALSO IMPACT NOT ONLY THOSE WITH TBI, BUT ALSO THOSE WITH SPINAL CORD INJURY, PARKINSON'S DISEASE, AND ALZHEIMER'S.

AS A SOCIAL WORKER ON THE FRONT LINES OF THIS BATTLE, I LOOK FORWARD TO THE DAY WHEN I CAN REFER MY PARTICIPANTS TO CELLULAR TBI CLINICAL TRIAL INSTEAD OF JUST REFERRING THEM TO BRAIN BANKS TO

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SUPPORT RESEARCH. THANK YOU FOR YOUR TIME.

MR. SHEEHY: THANK YOU. SO ADDITIONAL PUBLIC COMMENT?

DR. CUMMINGS: THANK YOU. SO I'M DR. CUMMINGS. I AM THE VICE CHAIR FOR RESEARCH IN PHYSICAL MEDICINE AND REHABILITATION AND NEUROLOGICAL SURGEON AT UC IRVINE, AND I'M SPEAKING ON BEHALF OF MY GRANT, 11548.

230,000 CALIFORNIANS AND $9 BILLION SPENT EVERY YEAR. EVERY DECADE THAT'S 2.3 MILLION ADDITIONAL CALIFORNIANS ARE AFFECTED AND 9 BILLION MORE IS LOST. THIS IS THE COST OF TRAUMATIC BRAIN INJURY JUST TO CALIFORNIA. TBI IS A SILENT EPIDEMIC AND THE LEADING CAUSE OF DEATH AND DISABILITY WORLDWIDE. FORTY PERCENT OF PATIENTS HAVE LONG-TERM DISABILITIES, INCLUDING MEMORY PROBLEMS AND ANXIETY. AND OUR TRAN1 WILL ADDRESS THESE SYMPTOMS AND THEIR PROHIBITIVE COST.

THERE ARE NO APPROVED THERAPIES FOR BRAIN INJURIES, AND BRAIN INJURIES INCREASE THE RISK OF SUBSEQUENT ALZHEIMER'S DISEASE. SO TREATING BRAIN INJURIES NOW COULD ULTIMATELY REDUCE ALZHEIMER'S AS WELL.

IN 2011 CIRM FUNDING HELPED EXPAND OUR SPINAL CORD WORK TO BRAIN INJURIES WITH AN EARLY

TRANSLATION AWARD, AND WE WERE SUCCESSFUL. IN 2016 A CIRM DISCOVERY AWARD ENABLED US TO VALIDATE A LEAD CANDIDATE FROM TWO FETAL AND TWO EMBRYONIC CELL LINES. OUR TRAN1 PROGRAM WILL COMPLETE GMP MANUFACTURE, ENABLE LONG-TERM SAFETY TESTING, AN ADD A LARGE ANIMAL MODEL USING OUR LEAD CANDIDATE, NOT A SURROGATE. WE ARE THE ONLY CIRM-FUNDED PROGRAM ADDRESSING TBI. WE HAVE SHOWN EFFICACY IN FOUR SEPARATE EXPERIMENTS USING CELLS FROM THREE MANUFACTURING RUNS. WE'VE IMPROVED LEARNING AND MEMORY AND REDUCED ANXIETY-LIKE BEHAVIOR TO TBI MODELS REPEATEDLY, AND WE HAVE DEMONSTRATED EFFICACY USING FROZEN VIALS OF CELLS. FRESHLY THAWED CELLS WILL FACILITATE THE SURGICAL APPROACH TO CLINICAL TRANSLATION USING OUR INTENDED CELLULAR PRODUCT. AGAIN, NOT A SURROGATE. AND, IMPORTANTLY, OUR LEAD CANDIDATE HAS A LARGER EFFECT SIZE THAN ANYTHING PREVIOUSLY REPORTED FOR BRAIN INJURY.

OUR LEAD CANDIDATE HAS FOUR MECHANISMS OF ACTION FROM CELL REPLACEMENT, NEUROGENESIS, NEUROPROTECTION, TO REDUCING INFLAMMATION. THIS INCREASES THE LIKELIHOOD OF TRANSLATION TO PEOPLE AS ONLY ONE NEEDS TO WORK. IT ALSO INCREASES THE POTENTIAL TO TREAT OTHER NEURODEGENERATIVE DISORDERS SUCH AS ALZHEIMER'S, PARKINSON'S, SPINAL CORD

INJURY, AND ALS.

THE CIRM'S GRANT WORKING GROUP HAS RECOMMENDED OUR TBI PROGRAM FOR FUNDING SEVERAL TIMES. WE'VE ONLY BEEN FUNDED TWICE. IN 2016 CIRM WAS SHORT OF FUNDS AND OUR DISC2 WAS SKIPPED OVER DESPITE A TIER I RECOMMENDATION. WE WERE ALSO RECOMMENDED FOR FUNDING BY THE DEPARTMENT OF DEFENSE BUT WAS CANCELLED ADMINISTRATIVELY TO AVOID THE CONTROVERSY OF EMBRYONIC STEM CELLS. CIRM IS THE ONLY AGENCY CAPABLE OF FUNDING THIS WORK, AND YOU'VE INVESTED MILLIONS IN OUR PROGRAM THUS FAR. CIRM SHARED IN THE INTELLECTUAL PROPERTY PORTFOLIO OF OUR LEAD CANDIDATE AND REVENUE SHARING FROM WHAT IS TRAGICALLY A HUGE MARKET. BRAIN INJURIES IMPACT MORE CALIFORNIANS THAN ALL OF THE OTHER TRAN GRANTS CURRENTLY UNDER CONSIDERATION.

FINALLY, WE NOTE THAT OUR WORK OVER THE LAST EIGHT YEARS HAS BEEN SUPPORTED BY CIRM BRIDGES INTERNS, TEN OF THEM, FOUR WHO REMAINED IN THIS TRAN1 GRANT. WITHOUT THESE INTERNS, OUR WORK COULD NOT HAVE BEEN COMPLETED. OUR TEAM HAS THE EXPERIENCE FOR MULTIPLE CLINICAL TRIALS USING CELL THERAPIES; AND IF SUCCESSFUL, WILL CONFRONT AN UNMET MEDICAL NEED FOR MILLIONS OF CALIFORNIANS AND THEIR FAMILIES AND POTENTIALLY SAVE CALIFORNIA BILLIONS IN

MEDICAL COSTS. AND IF WE SUCCEED, CIRM, WE WILL BE FUELING PUBLIC SUPPORT FOR RENEWAL IN 2020 BY ADDRESSING A CONDITION THAT EVERYONE CAN IDENTIFY WITH. THANK YOU.

MR. SHEEHY: ADDITIONAL PUBLIC COMMENT?

DR. NISTOR: MY NAME IS GABRIEL NISTOR. I'M THE CHIEF SCIENCE OFFICER AND HAVE CO-FOUNDED AIVITA, AND I'M HERE TO SUPPORT DR. CUMMINGS' APPLICATION. IF FUNDED, AIVITA WILL ACT AS A CONTRACTOR TO MANUFACTURE THE CELLS FOR THIS PROJECT. AND I'M HONORED TO BE HERE, AND SINCERELY I'M IMPRESSED. THIS IS THE FIRST TIME MY PARTICIPATION IN THIS KIND OF MEETING, AND I WISH I WAS HERE MORE ACTUALLY AND LISTENING TO ALL THESE COMMENTS AND THE DISCUSSION OF THE GRANTS.

SO AIVITA IS THE MAJOR ROADBLOCK IN DEVELOPING CELL THERAPY IN THE SCALE-UP WITH THE QUALITY WHICH ACTUALLY ALLOWS PRODUCT, WHICH GOES THROUGH FDA, AND ULTIMATELY IS APPROVED. AND WE'VE BEEN FOCUSING ON THESE ASPECTS FOR THE PAST 14, 15 YEARS.

WE HAVE IN THE SENIOR MANAGEMENT IN THE LEADERSHIP RENOWN WHICH ACTUALLY BROUGHT ALREADY CELL THERAPY PRODUCTS TO MARKET. AND THE REASON WE PARTICIPATING IN THIS APPLICATION IS BECAUSE WE SEE

A ROAD FORWARD. SO WE DO HAVE A PAVED ROAD. WE HAVE ABOUT -- WE HAVE FOUR CURRENT TRIALS IN PHASE 2 FOR CANCER. THEY'RE CELL THERAPIES, AUTOLOGOUS, ONE IN OVARIAN, ONE IN GBM, ANOTHER ONE IN MELANOMA IN JAPAN, AND ANOTHER ONE, A COMBINATION THERAPY OF MELANOMA AND CHECKPOINT INHIBITORS.

WE HAVE MANY, MANY INTERACTIONS WITH FDA, AND WE KNOW EXACTLY HOW THE ROAD IS MOVING FORWARD FOR THESE KIND OF APPROACHES.

WE ARE A COMPANY WHICH IS WELL FUNDED, WELL EQUIPPED. WE CAN PRODUCE ALL THE CELLS. WE CAN TAKE ANY EXTRA (UNINTELLIGIBLE), AND, MOST IMPORTANT, WE DO HAVE THE INVESTORS WHICH ARE ACTUALLY INTERESTED IN MOVING THESE PROGRAMS FORWARD. SO I URGE THIS COMMITTEE TO CONSIDER DR. BRIAN CUMMINGS' APPLICATION FOR FUNDING, AND I WON'T GO IN THE IMPORTANCE OF ADDRESSING IN OUR SOCIETY AFTER THIS CANCER SOLDIERS AND MEMBERS OF FAMILIES SUFFERING FROM BRAIN TRAUMA. THANK YOU VERY MUCH.

MR. SHEEHY: THANK YOU. ANY ADDITIONAL PUBLIC COMMENT? OKAY. AT THIS POINT PUBLIC COMMENT IS --

MR. MC CORMACK: THIS IS A COMMENT FROM DON REED. "HONORABLE MEMBERS OF THE -- I CAN'T

CONVEY HIS ENTHUSIASM, BUT I'LL TRY.

"HONORABLE MEMBERS OF THE ICOC, THANK YOU FOR ALLOWING ME TO MAKE PUBLIC COMMENT ON APPLICATION TRAN1-11579, THE HUMAN EMBRYONIC STEM CELL-DERIVED NEURAL STEM CELLS FOR SEVERE SPINAL CORD INJURY.

"MORE THAN 20 YEARS AGO DR. MARK TUSZYNSKI WAS ONE OF THE FIRST RECIPIENTS OF A ROMAN REED GRANT FOR SPINAL CORD INJURY RESEARCH. EVER SINCE, HE'S BEEN WORKING QUIETLY AND STEADILY IN TANDEM WITH THE FIELD OF REGENERATIVE MEDICINE. HIS PROJECT TO DATE, TRAN1-11579, IS THE CULMINATION OF THAT LIFETIME OF HARD WORK AND SCIENCE. I MEAN IT'S SPECTACULAR.

"USUALLY WHEN I SEE A PHOTOGRAPH OF A SPINAL CORD INJURY, IT'S HARD FOR ME TO UNDERSTAND WHAT'S GOING ON, COMPLICATED X-RAY OF THE SPINE, AND THE SCIENTIST POINTS TO A V-SHAPED LITTLE MARK AND SAYS THAT'S THE INJURY. AND SEE THAT LITTLE FUZZY GROWTH ON THE EDGES OF THE WOUND, THAT'S IT. THAT'S THE REGENERATION. AND I NOD MY HEAD AND SMILE, BUT IT TAKES A LOT OF FAITH TO SEE ANYTHING THERE.

"DR. TUSZYNSKI'S WORK IS DIFFERENT. IT'S IMPOSSIBLE NOT TO SEE NEW GROWTH. GREEN MARKS THE NERVES LEAPING ACROSS THE GAP IN THE INJURED SPINAL

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CORD REACHING TO THE OTHER SIDE AND NEW NERVE CELLS ARE BIOMARKED WITH GREEN SO YOU COULD FOLLOW THEM. IT WAS LIKE THE WHOLE SPINE WAS SLAVERED WITH LIME GREEN PAINT.

"WHAT DOES THAT MEAN IN PRACTICAL TERMS? IS THERE ANY RECOVERED MOTION? 'INJURED RATS WITH COMPLETELY SEVERED SPINAL CORDS RECOVERED SIGNIFICANT MOTION, INCLUDING THE ABILITY TO MOVE EVERY JOINT OF THEIR LEGS,' SAYS DR. TUSZYNSKI. THAT WAS IN RATS. HE'S SINCE GONE ON TO ACHIEVE SIMILAR RESULTS OF A NONHUMAN PRIMATE, A RHESUS MONKEY. MAJOR WORK HAS HONORED HIM BY PUBLISHING NO LESS THAN SIX ARTICLES ON HIS RECENT WORK, ARTICLES LIKE THE "STORAGE OF EFFECTS OF HUMAN NEURAL STEM CELL GRAFT WITH PRIMATE SPINAL CORD" AND "BIOMETRIC 3D PRINTED SPINAL CORD SCAFFOLD FOR SPINAL CORD INJURY," AND MOST RECENTLY "CHONDROITIN MAY HAVE IMPROVED ANATOMICAL AND FUNCTIONAL OUTCOMES AFTER PRIMATE SPINAL CORD INJURY," WHICH IS IN PRESS.

"HE'S DONE EVERY STEP OF THE EARLY WORK REQUIRED, ACHIEVED STRONG PRELIMINARY RESULTS. IT IS VITAL THAT HIS WORK CONTINUE, AND I URGE HIS CONTINUED SUPPORT. THANK YOU."

MR. SHEEHY: THANK YOU. THAT CLOSES PUBLIC COMMENT. WE HAVE A MOTION TO APPROVE 11579,

11548, AND 11628.

MS. BONNEVILLE: THE OTHERS OPEN UNTIL THE NEXT --

MR. SHEEHY: THAT WAS NOT THE MOTION.

MS. BONNEVILLE: OKAY.

DR. PRIETO: AS THE MAKER, I'D ACCEPT THAT AS A FRIENDLY AMENDMENT IF IT'S REQUIRED.

MR. SHEEHY: AND I THINK I SECOND, SO WE'D DO THAT BECAUSE I BELIEVE I WAS THE SECOND. SO WE WOULD TAKE THAT AS A FRIENDLY AMENDMENT TO HOLD ALL THE APPLICATIONS OPEN WITH THE ANTICIPATION OF MEETING WITH THE FULL BOARD TO REDIRECT FUNDS IN SEPTEMBER TO ALLOW US TO FUND THE REMAINING APPLICATIONS. SO COULD YOU CALL THE ROLL PLEASE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: DAVID HIGGINS. YOU'RE ON MUTE, DAVID. STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

MS. BONNEVILLE: DAVE MARTIN.

DR. MARTIN: YES.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES.

MS. BONNEVILLE: AL ROWLETT. JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
DR. HIGGINS: I'M BACK ON. I WANT TO SAY YES.
MS. BONNEVILLE: VOTE?
DR. HIGGINS: YES.
MS. BONNEVILLE: AL ROWLETT. I THINK YOU'RE ON MUTE.
MOTION CARRIES.
MR. SHEEHY: THANK YOU. AND I JUST WANT TO REITERATE THE REMAINING THREE APPLICATIONS ARE NOT DENIED FUNDING. THEY ARE OVERWHELMINGLY LIKELY TO BE FUNDED, AND THEY ARE ONLY BEING DELAYED A FEW MONTHS. AND IT DOES IN NO WAY REFLECT ON THE QUALITY OF THE SCIENCE.
BUT I WOULD, JUST AS AN EDITORIAL COMMENT, WHICH I THINK I CAN GET AWAY WITH MAKING BECAUSE THERE'S NOT AN EXISTING FORMAL CAMPAIGN TO RENEW THIS AGENCY, BUT ALL OF YOU BEING HERE TODAY IS AN

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EXAMPLE OF HOW IMPORTANT THE WORK WE DO IS. AND THE REALITY IS IT WILL TAKE EVERYBODY WHO'S BEEN INVOLVED WHO'S SEEN WHAT WE'VE ACCOMPLISHED, WHO HAVE HOPE FOR THE FUTURE AND WHAT WE CAN ACCOMPLISH.

WE JUST HEARD ABOUT CHALLENGES GETTING EMBRYONIC STEM CELLS FUNDED WITH THE FEDERAL GOVERNMENT. WE KNOW THAT WE HAVE TWO OUTSTANDING APPLICATIONS FOR FETAL TISSUE. I LOST MY MOTHER TO OVARIAN CANCER, SO I KNOW EXACT -- STAGE III. I KNOW EXACTLY THE STAGE IN WHICH THIS PARTICULAR INVESTIGATOR WANTED TO TARGET THE CANCER, AND I KNOW THE DIFFERENCE THAT THAT HAS THE POTENTIAL TO MAKE IN THE LIVES OF OVARIAN CANCER PATIENTS WHO INEVITABLY IN SO MANY CIRCUMSTANCE END UP HAVING AN INCREDIBLY PAINFUL, DIFFICULT ROAD. I WALKED THAT ROAD WITH MY MOM. THE HOPE THAT WE OFFER, THE CURES THAT WE ARE ALREADY PROVIDING, AND I'M GLAD WE HAVE DR. KUO FROM DR. KOHN'S LAB WHO'S CURED ALMOST 40 PATIENTS WITH A COUPLE OF INDICATIONS VIA CIRM FUNDING.

THIS IS REAL, BUT WE CANNOT ACCOMPLISH THE NEXT STAGE OF OUR MISSION WITHOUT THE SUPPORT OF THE PEOPLE WE'VE BEEN WORKING WITH ALL THESE YEARS. SO THANK YOU. AND IT HAS BEEN WONDERFUL TO HEAR FROM EVERYBODY TODAY, AND I AM COMMITTED MYSELF TO MAKING

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SURE THE REST OF THE APPLICATIONS GET FUNDED. THE SCIENCE HAS BEEN OUTSTANDING, AND IT'S AN HONOR TO RECEIVE THESE APPLICATIONS AND TO DO THIS WORK. SO THANK YOU. AND THANK YOU, CHAIRMAN THOMAS, FOR --

CHAIRMAN THOMAS: THANK YOU VERY MUCH, MR. SHEEHY, FOR BOTH THE INSPIRATIONAL WORDS AND NAVIGATING THROUGH THIS MEETING. IT WAS NOT EASY.

AND I'D LIKE TO ECHO ALL THE COMMENTS TO DRIVE HOME EXACTLY THE POWER OF THE TECHNOLOGY THAT YOU ALL ARE DEVELOPING AND WE HAVE HAD THE PRIVILEGE OF BEING ABLE TO FUND OVER THE YEARS AND HOPE TO AS THINGS GO FORWARD. SO THANKS TO EVERYBODY.

ARE THERE ANY PUBLIC COMMENTS ON ANY TOPICS OF ANY NOTE ON ANYTHING? HEARING NONE, I'D JUST LIKE TO CLOSE BY ONE LAST THING TO MENTION. IT MAY HAVE GONE UNNOTICED WHEN DR. CHIU WAS TALKING THAT SHE WAS RECENTLY AT CITY OF HOPE. THAT IS TO SAY THAT AFTER A VERY LONG AND DISTINGUISHED CAREER, WHICH HOPEFULLY PERHAPS WILL HAVE ANOTHER STAGE TO IT, THAT SHE IS RETIRED FROM CITY OF HOPE.

DR. CHIU WAS INSTRUMENTAL IN THE EARLY DAYS OF CIRM WORKING HERE, PROVIDING GREAT GUIDANCE ON MANY FRONTS, AND HAS DONE A LENGTHY LIST OF VERY IMPORTANT AND COMMENDABLE THINGS OVER THE YEARS, AND I DIDN'T WANT IT TO GO WITHOUT NOTICE.

AND, ARLENE, CONGRATULATIONS ON EVERYTHING YOU'VE DONE, NOT JUST FOR CIRM, BUT FOR EVERYWHERE YOU'VE BEEN. YOU'VE BEEN A TREMENDOUS HELP TO MANY, MANY PEOPLE. SO CONGRATULATIONS ON A WONDERFUL CAREER.

MR. TORRES: HERE. HERE.

(APPLAUSE.)

CHAIRMAN THOMAS: WITH THAT, WE STAND ADJOURNED. WE WILL SEE YOU IN AUGUST. THANK YOU.

(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 JULY 24, 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, CA CSR 7152
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