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

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: SEPTEMBER 1, 2023
11 A.M.

REPORTER: BETH C. DRAIN, CA CSR
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SEPTEMBER 1, 2023; 11 A.M.

CHAIRMAN GOLDSTEIN: OKAY. THEN, LANA, CAN YOU CALL THE ROLL. AND WE HAVE A SUBSTITUTE, MONICA CARSON, AND WILL BRIEFLY INTRODUCE HERSELF AT THAT POINT, AND THEN PICK UP AFTER THAT.

MS. MORALEZ: HAIFAA ABDULHAQ. MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MS. MORALEZ: MONICA CARSON.

DR. CARSON: PRESENT. MONICA CARSON, I'M PROFESSOR AND CHAIR OF BIOMEDICAL SCIENCES AT UC RIVERSIDE SCHOOL OF MEDICINE. AND JUST MY EXPERTISE OF HERE, I THINK LONG-TERM INTEREST IN NEURO-INFLAMMATION. I'M EDITOR IN CHIEF OF THE JOURNAL OF NEURO-INFLAMMATION.

CHAIRMAN GOLDSTEIN: THANK YOU.

MS. MORALEZ: ELENA FLOWERS. MARK FISCHER-COLBRIE.

MR. FISCHER-COLBRIE: HERE.

MS. MORALEZ: JUDY GASSON.

DR. GASSON: HERE.

MS. MORALEZ: LARRY GOLDSTEIN.

CHAIRMAN GOLDSTEIN: I'M HERE.

MS. MORALEZ: DAVID HIGGINS.

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DR. HIGGINS: PRESENT.

MS. MORALEZ: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: PRESENT. AND WELCOMING MONICA.

MS. MORALEZ: PAT LEVITT.

DR. LEVITT: PRESENT.

MS. MORALEZ: SHLOMO MELMED. CHRISTINE MIASKOWSKI.

DR. MIASKOWSKI: PRESENT.

MS. MORALEZ: KAROL WATSON. KEITH YAMAMOTO.

DR. YAMAMOTO: HERE.

CHAIRMAN GOLDSTEIN: OKAY. THANK YOU, LANA. THANK YOU ALL WHO ARE ATTENDING.

WE HAVE A LIVELY AND INTERESTING AGENDA TODAY. THE FIRST ITEM THAT WE'RE GOING TO TAKE UP IS CONSIDERATION OF A CONCEPT PLAN CALLED REMIND THAT ROSA CANET-AVILES AND HER COLLEAGUES HAVE DEVELOPED TO DEVELOP A GRANTING PROGRAM FOR NEUROPSYCHIATRIC DISEASE AS YOU WILL SEE.

BEFORE WE GET TO THAT, I WANT TO JUST GIVE YOU SOME CONTEXT AND BACKGROUND FOR WHERE THIS HAS EMERGED BECAUSE IT CAME FROM THE TASK FORCE ON NEUROSCIENCE AND NEUROMEDICINE THAT WE'VE BEEN DEVELOPING. I'M GOING TO SHARE MY SCREEN. YOU ALL

WERE ABLE TO DOWNLOAD THE DOCUMENT THAT WE POSTED, I HOPE. IT STARTS WITH A CHARGE TO THE TASK FORCE ON NEUROSCIENCE AND NEUROMEDICINE. AND I WANT TO START WITH THAT BECAUSE THERE ARE TWO KEY POINTS THAT PART OF THE CONTEXT FOR THE CONCEPT PLAN THAT WE'LL BE EVALUATING.

THE FIRST IS THAT THE TASK FORCE NEEDS TO DEVELOP A GENERAL PLAN FOR THE ONE AND A HALF BILLION SET-ASIDE THAT WAS STATED IN PROP 14, ONE AND A HALF BILLION OUT OF FIVE AND A HALF BILLION. AND WE'RE WORKING AWAY ON THAT GENERAL PLAN. AND I'LL GIVE YOU JUST A BRIEF UPDATE OF THAT IN A MOMENT.

AND THEN THE SECOND ITEM THAT'S VERY IMPORTANT IN OUR CHARGE IS THAT WE ARE CHARGED TO IDENTIFY UNUSUAL OPPORTUNITY FOR HIGH IMPACT IN THESE AREAS FOR ENHANCED INVESTMENT. AND THAT STATEMENT IS, AS YOU WILL SEE, THE BASIS FOR A CONCEPT PLAN FOR NEUROPSYCHIATRIC DISEASE THAT WE'LL SEEING -- THAT ROSA WILL BE PRESENTING IN A FEW MINUTES.

NOW, TO GIVE YOU A SENSE OF WHAT OUR PROGRESS HAS BEEN, FIRST, AS INDICATED IN THE FIRST COUPLE SENTENCES HERE, IF YOU LOOK AT OR JUST DO THE SIMPLE ARITHMETIC OF ONE AND A HALF OUT OF FIVE AND

A HALF BILLION, IT'S ABOUT A 27-PERCENT FRACTION THAT'S MANDATED BY PROP 14. AND SIMPLY CIRM USING THE GRANTS WORKING GROUP TO SELECT AMONG THE SUBMITTED PROPOSALS, THUS FAR IT'S RUNNING AT ABOUT THE RIGHT FRACTION. SO IN PRINCIPLE, IF I WE DID NOTHING, WHICH I'M NOT SUGGESTING WE DO, WE'VE HIT THE RIGHT. BUT THERE ARE SOME REALLY INCREDIBLE OPPORTUNITIES THAT THIS CHARGE OPENS UP.

AND ONE OF THE THINGS THAT WAS IMPORTANT THAT WE LEARNED FROM A BRIEF PORTFOLIO ANALYSIS THAT CIRM PUT TOGETHER IS THAT NEUROPSYCHIATRIC DISEASE, WHICH HAS JUST BECOME TRACTABLE WITH STEM CELL TECHNOLOGIES, IN MY VIEW, MORE ABOUT THAT IN A MOMENT, TURNS OUT WAS COMPLETELY UNDERREPRESENTED IN THE CIRM PORTFOLIO. THERE WERE ZERO GRANTS THAT HAD BEEN MADE IN THIS AREA. AND USING DALY, DISABILITY ADJUSTED LIFE YEAR BURDEN, WHICH IS ONE WAY OF LOOKING AT IMPACT OF A DISORDER, THE DALY NUMBER JUST DWARFED EVERY OTHER NEURO DISEASE THAT WE HAVE BEEN FUNDING. AND SO IT'S A VERY STRAIGHTFORWARD COMBINATION OF A HIGH BURDEN. AND WE DON'T HAVE MUCH OF A PRESENCE IN THAT AREA.

AND WHAT WE DID WAS REALLY VET THE AREA. SO WE HAD A SERIES OF EXPERTS IN THE TECHNOLOGIES AND IN NEUROPSYCHIATRIC DISEASE COME IN AND TALK TO

US OVER THE COURSE OF SEVERAL MEETINGS. AND THEY ESTABLISHED THAT STEM CELL TECHNOLOGIES AND RELATED TECHNOLOGIES HAVE REALLY REACHED THE POINT WHERE ALONG WITH BETTER UNDERSTANDING OF THE GENETICS OF NEUROPSYCHIATRIC DISEASE, A REALLY TERRIFIC OPPORTUNITY HAS PRESENTED ITSELF FOR US TO POTENTIALLY MAKE AN IMPACT. AND YOU'LL HEAR MORE ABOUT THAT FROM ROSA IN A MOMENT.

BUT IT'S VERY CLEAR THAT THERE'S ENOUGH GENETICS THAT RARE VARIANTS WITH STRONG EFFECTS HAVE BEEN IDENTIFIED AS WELL AS MULTIPLE MORE COMMON VARIANTS WITH SMALLER IMPACT, A PIECE, BUT TOGETHER IN ONE PERSON CAN REALLY MAKE A DIFFERENCE IN THEIR SUSCEPTIBILITY TO DISEASE. IN THAT SENSE, IT'S LIKE A LOT OF SO-CALLED SPORADIC DISEASES THAT WE ALL KNOW AND WOULD LIKE TO DEVELOP THERAPIES FOR.

FINALLY, ROSA WILL NOW TELL YOU ABOUT A CONCEPT PLAN FOR THIS AREA THAT WE THINK MAKES IT ATTRACTIVE FOR WORKERS IN THIS AREA TO PUT TOGETHER INTERDISCIPLINARY TEAMS TO WORK ON THESE PROBLEMS AND, IN OUR VIEW, WILL ATTRACT CIRM SUPPORT GIVEN THE IMPORTANCE OF THE AREA AND THE QUALITY OF THE TECHNOLOGIES THAT CURRENTLY EXIST.

SO THAT'S ALL I WANT TO SAY IN TERMS OF PREAMBLE. UNLESS ANYBODY HAS A QUESTION, WHAT I'D

LIKE TO DO NOW IS TURN THE PODIUM OR WHATEVER THIS IS OVER TO ROSA TO PRESENT THE CONCEPT PLAN. SHE'LL PRESENT, WE'LL THEN TAKE QUESTIONS, I'LL THEN ASK FOR A MOTION TO PASS, WE'LL HAVE FURTHER AND FINAL DISCUSSION, PUBLIC COMMENT, AND THEN WE'LL VOTE. SO THAT WILL BE THE PROGRESSION OF HOW WE'RE GOING TO WORK.

SO LET ME STOP SHARING MY SCREEN AND GO BACK TO THE MAIN SCREEN. ROSA, ARE YOU READY? YOU ARE.

DR. CANET-AVILES: WE ARE READY. I WOULD LIKE TO THANK YOU, DR. GOLDSTEIN AND THE MEMBERS, FOR SUCH A WONDERFUL SUMMARY AND ALSO TO THE MEMBERS OF THE SCIENCE SUBCOMMITTEE FOR THE OPPORTUNITY TO PRESENT THE CONCEPT FOR THIS FIRST NEURO PROGRAM, FOCUSED DISCOVERY PROGRAM.

SO THE PRESENTATION TODAY IS GOING TO BE A SPLIT BETWEEN ME AND DR. CHAN LEK TAN, WHO IS A SENIOR SCIENCE OFFICER IN OUR TEAM AND WHO HAS BEEN ALSO WORKING ON THE DEVELOPMENT OF THIS CONCEPT.

SO AS YOU KNOW, THE NEURO DISCOVERY PROGRAM, ALSO KNOWN AS REMIND, WHICH STANDS FOR RESEARCH USING MULTIDISCIPLINARY, INNOVATIVE APPROACHES IN NEURO DISEASES, IS PART OF THE TASK FORCE EFFORTS TO IDENTIFY UNUSUAL OPPORTUNITIES FOR

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HIGH IMPACT IN NEUROSCIENCE AREAS FOR ENHANCED INVESTMENT BY THE STEM CELL AGENCY IN CALIFORNIA.

FOR THOSE MEMBERS THAT WERE NOT ABLE TO ATTEND LAST FRIDAY'S TASK FORCE ON NEUROSCIENCE AND NEUROMEDICINE, THIS CONCEPT HAS BEEN DEVELOPED OVER THE PAST EIGHT MONTHS AND INCORPORATED ALL THE INPUT AND FEEDBACK FROM THE TASK FORCE.

THIS PRESENTATION IS A COMPLEMENT TO THE CONCEPT DOCUMENT THAT WAS DISTRIBUTED LAST FRIDAY AND CONTAINS THE BACKGROUND AND DETAILS COMPLEMENTARY TO THIS PRESENTATION.

SO JUST AS A REMINDER, THE REMIND INITIATIVE CORRESPONDS TO THE DISCOVERY PHASE OF CIRM'S NEURO STRATEGY. AND THE TRANSLATION AND CLINICAL AREAS WILL BE ADDRESSED SEPARATELY.

CIRM'S NEUROSCIENCE STRATEGY HAS BEEN DEVELOPED IN THE CONTEXT OF OUR MISSION STATEMENT, WHICH IS TO ACCELERATE WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO A DIVERSE CALIFORNIA AND THE WORLD. AND IT INTEGRATES WITHIN OUR FIRST THEME OF ADVANCING WORLD-CLASS SCIENCE.

THE VISION OF THE REMIND PROGRAM HAS BEEN INFORMED BY MULTIPLE STAKEHOLDER DISCUSSIONS OF THE PAST YEARS AS I MENTIONED. AND THE GOAL OF THIS

PROGRAM REFLECTS INCORPORATION OF ALL MAJOR TAKEAWAYS FROM THIS DISCUSSION, INCLUDING THE PAST EIGHT MONTHS. THE GOAL IS TO ACCELERATE THE DISCOVERY OF MECHANISMS UNDERLYING NEUROPSYCHIATRIC DISORDERS LEADING TO THE IDENTIFICATION AND VALIDATION OF NOVEL TARGETS AND BIOMARKERS WITH A GOAL TO PROVIDE NEW AVENUES AND RIGOROUS FOUNDATIONS FOR FUTURE TRANSLATIONAL AND CLINICAL INVESTIGATIONS.

AND THE SPECIFIC OBJECTIVES TO ACHIEVE THESE GOALS ARE TO ACCELERATE FOUNDATIONAL SCIENTIFIC UNDERSTANDING OF NEUROPSYCHIATRIC DISEASE MECHANISMS, ALSO DEVELOP RELEVANT, INFORMATIVE TOOLS OR TECHNOLOGIES THAT WILL ULTIMATELY HELP US ACCELERATE THE UNDERSTANDING OF THESE DEVASTATING DISEASES. TO CATALYZE MULTIDISCIPLINARY INNOVATION, ATTRACTING NEW TALENT AND IDEAS INTO NEUROPSYCHIATRIC RESEARCH AND SEEDING NEW PARTNERSHIPS, AND TO DRIVE OPEN AND COLLABORATIVE SCIENCE BY LEVERAGING CIRM-FUNDED AND ALSO EXTERNALLY FUNDED INFRASTRUCTURE FOR DATA, RESOURCES, AND KNOWLEDGE SHARING.

SOME OF THE WORK OF THE NEURO TASK FORCE OVER THE PAST FEW MONTHS HAS BEEN DISCUSSIONS AROUND THE WAYS IN WHICH WE CAN ACHIEVE THESE GOALS AND

OBJECTIVES. AND THE PROGRAM STRUCTURE ACTUALLY ANSWERS TO THESE OBJECTIVES OF ENABLING MULTIDISCIPLINARY LARGE TEAMS TO WORK TOGETHER AND INCORPORATES ALL THE FEEDBACK FROM THE PAST MONTH'S DISCUSSIONS, INCLUDING ALLOWING FOR A LARGER AMOUNT OF TIME TO DO THE WORK AND LARGER AMOUNTS OF FUNDING.

THE STRUCTURE OF THIS INITIATIVE PROGRAM RESPONDS TO THOSE PRIORITIZATION ELEMENTS AND INCLUDES TWO FUNDING OPPORTUNITIES WITH DISTINCT AWARD STRUCTURES THAT WILL BE OFFERED THROUGH INDEPENDENT REQUESTS FOR APPLICATIONS OR RFA'S.

THE FIRST ONE, THE REMIND-L, L STANDING FOR LARGE, COLLABORATIVE TEAMS, WILL SUPPORT EXPANSIVE, CROSS-DISCIPLINARY STUDIES LED BY LARGE COLLABORATIVE TEAMS THAT WILL APPLY -- BY APPLYING A RANGE OF TECHNOLOGIES AND APPROACHES LEADING TO NOVEL BIOLOGICAL INSIGHTS, FURTHERING OUR CURRENT UNDERSTANDING OF DISEASE MECHANISMS, AND EXPANDING RESEARCH TO INCLUDE THE STUDY OF DIVERSE POPULATIONS AS WELL AS IDENTIFYING AND VALIDATING NOVEL THERAPEUTIC HYPOTHESES, TARGETS, OR BIOMARKERS.

THE OTHER REQUEST FOR APPLICATIONS PROGRAM IS THE REMIND-X RFA, WHICH WILL SUPPORT HIGH RISK EXPLORATORY, THAT'S WHAT THE X IS FOR, STUDIES LED

BY SMALL MULTIDISCIPLINARY TEAMS. THE PROJECTS, THE PROPOSED PROJECTS WILL BE EXPECTED TO LEAD TO INITIAL VALIDATION OR PROOF OF CONCEPT OF NOVEL MODELS, TOOLS, TECHNOLOGIES, OR HYPOTHESES.

FOR THE REMIND-L, WE PROPOSE FOUR YEARS WITH A BASE COMPONENT OF $2 MILLION A YEAR PER PROJECT AND UP TO $8 MILLION TOTAL IN DIRECTS WITH AN EXPECTED NUMBER OF SIX AWARDS AWARDED. FOR THE REMIND-X, CIRM EXPECTS TO FUND DIRECT PROJECT COSTS OF UP TO ONE MILLION TOTAL, HALF A MILLION DOLLAR PER AWARD PER YEAR, FOR UP TO TWO YEARS OF DURATION. AND WE ESTIMATE EXPECTED NUMBER OF 12 AWARDS.

NOW, THERE IS AN EXTRA OPTION FOR THE REMIND-L, THE LARGE COLLABORATIVE PROJECTS, THAT WE ARE PROPOSING, WHICH IS AN OPTION THAT COULD ALLOW FOR SUPPLEMENTAL FUNDING. IN THIS CASE, ADDITIONAL FUNDING OF UP TO HALF A MILLION DOLLARS PER AWARD PER YEAR MAY BE REQUESTED IF AN EQUIVALENT OR LARGER AMOUNT OF MATCHING FUNDS IS PROVIDED AND THE RESEARCH ACTIVITIES SUPPORTED BY THIS SUPPLEMENTAL BUDGET ARE DESCRIBED AND WILL BE WELL JUSTIFIED.

MATCHING FUNDS COULD BE CONTRIBUTED BY CALIFORNIA OR NON-CALIFORNIA FOR-PROFIT OR NONPROFIT ORGANIZATIONS. ONE OF THE INTENTIONS OF THIS MATCHING FUND IS TO INSTIGATE COLLABORATIVE EFFORTS

WITH EXTERNAL ORGANIZATIONS.

THE REMIND-X, WE'LL FUND DIRECT PROJECT COST -- SORRY. I'VE ALREADY SAID THAT.

SO FOR THE REMIND-L WITH THESE POTENTIAL MATCHING FUNDS, THE TOTAL AMOUNT, POTENTIAL AMOUNT FOR FUNDING PER YEAR IS UP TO $2.5 MILLION IN DIRECTS WITH A TOTAL OF $10 MILLION TOTAL AWARD IN FOUR YEARS. THIS CORRESPONDS TO $88.2 MILLION IF WE INCLUDE INDIRECTS AND FACILITIES COSTS AND $22.5 MILLION FOR THE REMIND-X PROJECT.

THIS IS A TIMELINE. THIS IS JUST TO SHOW THAT YOU CAN ESSENTIALLY THINK OF THIS AS STARTING THE PROGRAM IN 2024 AS YEAR ONE IN WHICH WE WOULD LAUNCH THE FIRST SET OF REMIND-L AWARDS AND THEN REMIND-X COULD BE LAUNCHING IN 2025.

NOW I'D LIKE TO INTRODUCE DR. CHAN LEK TAN, WHO'S BEEN WORKING IN THE DEVELOPMENT OF THIS CONCEPT AND WILL PRESENT SOME IMPORTANT SLIDES REGARDING ELIGIBILITY. CHAN.

DR. TAN: THANK YOU, ROSA. AND GOOD MORNING, EVERYONE. IN THE NEXT FEW SLIDES, I WILL SPEAK TO SOME OF THE SPECIFICS OF THE PROGRAMS STARTING WITH THE ELIGIBILITY REQUIREMENTS FOR APPLICANT TEAMS.

FIRSTLY, ALL NONPROFIT AND FOR-PROFIT

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CALIFORNIA RESEARCH ORGANIZATIONS ARE ELIGIBLE TO APPLY FOR THESE AWARDS. IN TERMS OF COMPOSITION, AS AGREED WITH THE TASK FORCE, ALL TEAMS WILL NOMINATE A SINGLE PRINCIPAL INVESTIGATOR WHO WILL MANAGE THE PROJECT AND SERVE AS THE PRIMARY CIRM CONTACT. IN ADDITION, THE TEAM MUST INCLUDE AT LEAST FOUR CO-INVESTIGATORS FOR REMIND-L AND AT LEAST ONE CO-INVESTIGATOR FOR REMIND-X.

IN TERMS OF INVESTIGATOR EFFORT AND IN AGREEMENT WITH TASK FORCE FEEDBACK AND AGREEMENT, PI'S FOR REMIND-L MUST DEVOTE AT LEAST 15 PERCENT EFFORT AND CO-INVESTIGATORS HAVE TO DEVOTE AT LEAST 10 PERCENT. FOR REMIND-X, BOTH PI AND CO-INVESTIGATORS HAVE A 5-PERCENT MINIMUM EFFORT REQUIREMENT.

LASTLY, IN TERMS OF TEAM COMPOSITION, WE ASK THAT AT LEAST ONE MEMBER OF THE OVERALL REMIND-L TEAM TO HAVE RELEVANT CLINICAL EXPERTISE AND ONE MEMBER TO HAVE RELEVANT COMPUTATIONAL OR RELATED EXPERTISE, AND SUCH MEMBERS CAN BE EITHER THE PI ITSELF OR CO-INVESTIGATORS OR OTHER KEY PERSONNEL. FOR REMIND-X WE WILL ENCOURAGE IN THE RFA APPLICATIONS FROM INVESTIGATORS WHO WILL BRING NEW TECHNOLOGIES, RESOURCES, OR FRAMEWORKS TO THE STUDY OF NEUROPSYCHIATRIC DISORDERS OR IN VITRO MODELS OF

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THE HUMAN CNS.

IN TERMS OF PROJECT ELIGIBILITY AND IN ALIGNMENT WITH OUR CONCEPT DOCUMENT, PROJECTS MUST ADDRESS A KNOWLEDGE GAP OR RESEARCH BOTTLENECK IN OUR UNDERSTANDING OF NEUROPSYCHIATRIC DISORDERS. PROJECTS MUST EMPLOY STEM CELLS OR GENETIC RESEARCH AS PART OF THE CENTRAL APPROACH. AS PART OF THIS MULTIDISCIPLINARY PROGRAM, WE ARE ENCOURAGING A MULTITUDE OF APPROACHES; HOWEVER, APPLICANTS WILL NEED TO JUSTIFY SEGMENTS OF THE OVERALL PROJECT THAT DOES NOT DIRECTLY INVOLVE STEM CELL OR GENETIC APPROACHES. FOR EXAMPLE, THEY WOULD JUSTIFY SUCH STUDIES IN TERMS OF HOW THEY MIGHT COMPLEMENT OR IMPROVE THE VALIDITY OF THE CENTRAL STEM CELL GENETIC APPROACH.

AND FINALLY, THE REMIND PROGRAM PRIORITIZES STUDIES BASED ON HUMAN DATA, HUMAN MODELS, AND HUMAN TISSUE SAMPLES ALTHOUGH STUDIES USING NONHUMAN MODELS WILL BE PERMITTED. WE DO ASK THAT TEAMS VALIDATE FINDINGS DERIVED FROM THESE APPROACHES USING HUMAN CELLS AND TISSUES DURING THE COURSE OF THE AWARD. AND AS SUGGESTED DURING THE PRIOR TASK FORCE DISCUSSION, THE RFA LANGUAGE WILL ALSO REFLECT THIS EMPHASIS ON HUMAN MODELS.

AND ON THE LAST SLIDE, DATA SHARING AND

KNOWLEDGE SHARING, AS ROSA SAID, IS KEY TO ADVANCING THE FIELD OF REGENERATIVE MEDICINE AND ACCELERATING THE DEVELOPMENT OF TREATMENTS. SINCE THE PASSAGE OF PROP 14, CIRM HAS IMPLEMENTED A SET OF GUIDELINES TO SHARE AND MANAGE DATA WITH A VISION TO SUPPORT THE BROADER COLLABORATIVE RESEARCH ECOSYSTEM THAT THE REMIND PROGRAM WILL BE A PART OF. AS SUCH, WE WILL BE REQUIRING DATA SHARING AND MANAGEMENT PLANS BASED ON CIRM GUIDELINES, AND WE WILL ALSO FACILITATE COORDINATION BETWEEN AWARDEES AND OTHER DATA INITIATIVES.

FINALLY, THE REMIND PROGRAM WILL ALSO UPHOLD THE PRINCIPLES OF DIVERSITY, EQUITY, AND INCLUSION, AND THE APPLICANTS WILL BE REQUIRED TO INCLUDE PLANS TO ADDRESS DEI CONSISTENT WITH THE OTHER PROGRAMS WITHIN CIRM'S OFFERINGS. AND WITH THAT, I'LL HAND IT BACK TO ROSA.

DR. CANET-AVILES: THANK YOU SO MUCH, CHAN.

FROM WHAT CHAN WAS TALKING ABOUT IS FACILITATING THE COORDINATION WITH INITIATIVES. THIS LEADS TO SHOWING HOW THE VISION OF THIS PROGRAM WILL LEAD TO ACCELERATING WORLD-CLASS SCIENCE AND TO FURTHER ACCELERATE THE DISCOVERY OF NOVEL INSIGHTS INTO MECHANISMS OF NEUROPSYCHIATRIC DISEASES. THE

REMIND PROGRAM, WHICH IS HERE SHOWN BY THESE LARGE PROJECT TEAMS AT THE EARLIER PROJECTS LIKE REMIND-X AND REMIND-L AIMS TO ESTABLISH COLLABORATIVE NETWORKS OF MULTIDISCIPLINARY RESEARCH TEAMS THROUGH NEW FUNDING STRUCTURES THAT ARE COMPLEMENTARY TO OUR CURRENT DISCOVERY STAGE AWARDS, WHICH ARE THE DISC-0 FOUNDATION AWARDS AND THE DISC2 QUEST AWARDS.

FURTHERMORE, WE HOPE THAT WE WILL BE ABLE TO LEVERAGE CIRM FUNDING INFRASTRUCTURE ELEMENTS, SUCH AS THE SHARED RESOURCE LABS, THE DATA COORDINATION AND MANAGEMENT CENTERS OR DATA INITIATIVES, AND OTHERS, AS WELL AS EXTERNAL CONSORTIA WHICH COULD BE LEADING ULTIMATELY TO DRIVING THE OBJECTIVES THAT WE WERE TALKING ABOUT INITIALLY OF CATALYZING COLLABORATION, DRIVING INNOVATION FROM THESE MULTIDISCIPLINARY TEAMS THAT COULD LEAD TO THE DISCOVERY OF NOVEL TARGETS AND BIOMARKERS AND INCREASING ULTIMATELY THE EFFICIENCY AND THE SUCCESS OF CLINICAL TRIALS FOR NEUROPSYCHIATRIC DISORDERS. THIS OVERALL CONNECTS OUR THREE PILLARS OF RESEARCH AND DEVELOPMENT FROM DISCOVERY TO TRANSLATION TO THE CLINICAL.

THIS LAST SLIDE OR ONE BEFORE THE LAST IS A SUMMARY OF THE PROGRAM BUDGET THAT REFLECTS THE CHANGES THAT WERE MADE BASED FROM THE TASK FORCE

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FEEDBACK. IN JUNE THE AGENCY'S RESEARCH BUDGET HAD A PLACEHOLDER OF $62.2 MILLION FOR THE REMIND CONCEPT PLAN, A NUMBER THAT AT THE TIME WAS UNDERSTOOD TO BE SUBJECT TO REVISION AS THE CONCEPT PLAN WAS STILL FURTHER REFINED WITH THE BENEFIT OF FURTHER WORK FROM THE NEUROSCIENCE AND NEUROMEDICINE TASK FORCE, THE ACTUAL PROGRAM BUDGET IS NOW CLEAR AND WILL REQUIRE 26 MILLION MORE FOR THE REMIND-L FISCAL YEAR 23/24 BUDGET, COMING UP TO 88.2 MILLION. AND THIS ADDITIONAL ALLOCATION WILL BE SOUGHT OF THE FULL BOARD AT THE SEPTEMBER ICOC CONSIDERATION OF THIS CONCEPT PLAN, ASSUMING, OF COURSE, THAT THIS SCIENCE SUBCOMMITTEE RECOMMENDS BRINGING THE CONCEPT TO THAT MEETING.

JUST AS A CLARIFICATION, THE REMIND-X BUDGET REQUEST WILL BE MADE NEXT YEAR AS PART OF THE FISCAL YEAR 24/25 RESEARCH BUDGET. SO THERE ARE NO CHANGES TO THE REQUEST FROM THE BOARD AT THIS TIME.

FINALLY, THE REQUESTED ACTION FROM THE SCIENCE SUBCOMMITTEE IS THAT CIRM REQUEST THE BOARD TO APPROVE THE PROPOSED REMIND PROGRAM CONCEPT.

WITH THAT, I WOULD LIKE TO LEAVE TIME FOR QUESTIONS. THANK YOU VERY MUCH FOR YOUR ATTENTION AND FOR YOUR SUPPORT.

CHAIRMAN GOLDSTEIN: THANK YOU, ROSA AND

CHAN. EXCELLENT PRESENTATION.

I'LL JUST ADD THAT THE TASK FORCE DID A VERY THOROUGH JOB OF WORKING WITH ROSA AND HER TEAM TO VET THIS CONCEPT PLAN. I'M NOT GOING TO CLAIM THAT IT THOUGHT OF EVERYTHING, BUT IT DEFINITELY MADE SOME GOOD SUGGESTIONS THAT ALTERED ITS COURSE.

SO QUESTIONS FROM THE SCIENCE SUBCOMMITTEE PLEASE. CHRISTINE.

DR. MIASKOWSKI: THANK YOU FOR THE EXCELLENT PRESENTATION. I HAVE TWO QUESTIONS. ONE IS RELATED TO WHY THE STAGGERED TIMELINE FOR THE TWO SETS OF PROJECTS? WHY CAN'T THEY START AT THE SAME TIME?

AND THEN MAYBE THIS ONE IS A LITTLE SELF-SERVING BY BEING ON THE GRANTS WORKING GROUP. WHO IS THE INTENDED REVIEW GROUP FOR THESE GRANTS? ARE YOU GOING TO INCORPORATE IT INTO OUR CURRENT STRUCTURE, OR ARE YOU INTENDING TO CREATE A SEPARATE REVIEW GROUP?

DR. CANET-AVILES: THANK YOU VERY MUCH FOR THE QUESTIONS. VERY RELEVANT, DR. MIASKOWSKI.

SO THEY ARE RELATED, BOTH QUESTIONS. THE REASON WHY THEY ARE STAGGERED IS BECAUSE THE SCOPE OF THE AWARDS IS VERY DIFFERENT. SO THE REVIEW TEAMS COULD BE VERY DIFFERENT. AND FOR CAPACITY OF

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THE REVIEW TIMELINES, WE HAVE SEPARATED THEM. ALSO, FOR CONSULTATIONS, THIS REQUIRES STAFF TO CONSULT AND TO WORK HAND IN HAND. AND OUR TEAM ALSO IS FOR CAPACITY PURPOSES, SO WE WANT TO DO A GOOD JOB. SO THAT'S THE ANSWER TO THE FIRST QUESTION.

THE SECOND IS, THE ANSWER, IF MY COLLEAGUE, DR. GIL SAMBRANO, DOESN'T MIND, I'LL ANSWER, BUT I'M HAPPY IF YOU WANT TO ADD ANYTHING ELSE, GIL. IT COULD BE THE SAME GRANTS WORKING GROUP PROCESS. HOWEVER, WE'VE BEEN RECRUITING NEW, NOT ONLY BECAUSE OF THIS INITIATIVE, BUT ALSO BECAUSE OF THE PROP 14'S MANDATE FOR NEUROSCIENCE, WE'VE BEEN ACTUALLY WORKING VERY ACTIVELY IN THE RECRUITMENT OF SPECIALIZED REVIEWERS, NOT ONLY FOR NEUROSCIENCE, BUT ALSO FOR COMPUTATIONAL BIOLOGY, DATA SCIENCES, ET CETERA. SO THE COMPOSITION WILL BE DIFFERENT, BUT IT WILL ALSO INCLUDE SOME OF THE DISCOVERY REVIEWERS, I IMAGINE.

GIL, DO YOU HAVE ANYTHING ELSE TO ADD?

DR. SAMBRANO: NO. THAT WAS ALL APPROPRIATE. THANK YOU.

DR. MIASKOWSKI: THANKS VERY MUCH.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU, ROSA AND GIL.

OTHER QUESTIONS FOR ROSA? SEEING NONE,

DOES ANYBODY WANT TO MAKE A MOTION TO RECOMMEND THAT WE SEND THIS ON TO THE FULL ICOC?

DR. MIASKOWSKI: SO MOVED.

CHAIRMAN GOLDSTEIN: I HEARD CHRISTINE'S VOICE, BUT I DON'T KNOW WHO THE OTHER ONE WAS.

DR. LEVITT: IT WAS PAT, BUT YOU CAN MARK DOWN CHRISTINE. SHE HAD A GOOD QUESTION. SHE DESERVES THE REWARD, BUT I CAN SECOND IT, RIGHT?

CHAIRMAN GOLDSTEIN: THAT'S RIGHT. YOU'LL HAVE TO SPLIT THE PRIZE MONEY. OKAY. GOOD.

ANY FURTHER DISCUSSION NOW THAT THIS HAS BEEN MOVED AND SECONDED?

DR. LEVITT: I JUST WANT TO ADD THAT, I DON'T THINK ROSA MENTIONED THIS, THAT THE STAFF DID REALLY AMAZING DUE DILIGENCE. NOT ONLY THE EXPERTS WHO CAME IN TO SPEAK TO THE NEUROSCIENCE WORKING GROUP, BUT ALSO ENGAGING WITH NIH AND OTHER FUNDERS WHO HAVE BEEN SPENDING MANY YEARS TRYING TO FIGURE OUT THE BEST WAYS OF PROVIDING SUPPORT TO MAKE BREAKTHROUGH DISCOVERY. SO THEY REALLY DID, I THINK, A REALLY THOROUGH JOB OF GETTING INPUT FROM A LOT OF DIFFERENT SOURCES TO COME UP WITH THIS PLAN. I JUST WANTED TO SAY THAT AND CONGRATULATE THE TEAM.

CHAIRMAN GOLDSTEIN: COMPLETELY AGREE. THANK YOU, PAT. JUDY.

DR. GASSON: I JUST WANT TO SECOND WHAT PAT SAID AS A FELLOW MEMBER OF THE NEUROSCIENCE TASK FORCE. I THINK ROSA AND CHAN AND THEIR TEAM REALLY INTERACTED WELL WITH THE MEMBERS OF THE TASK FORCE. AND I ALSO WANT TO THANK LARRY WHO DID A TERRIFIC JOB OVER THE EIGHT MONTHS OF BRINGING IN THE SPEAKERS, A LOT OF REALLY THOUGHTFUL DISCUSSION, AND DRIVING OUR GOAL TO REALLY HAVE AN IMPACT ON THESE VERY SERIOUS DISORDERS. SO THANKS TO ALL OF YOU. GREAT JOB.

CHAIRMAN GOLDSTEIN: THANK YOU, JUDY.

OTHER DISCUSSION POINTS FROM THE SCIENCE SUBCOMMITTEE PLEASE. OKAY. HEARING AND SEEING NONE --

VICE CHAIR BONNEVILLE: I THINK DAVID HAS A COMMENT.

CHAIRMAN GOLDSTEIN: OH. DAVID, PLEASE.

(A PAUSE IN THE PROCEEDING.)

DR. HIGGINS: OKAY. SORRY ABOUT THAT. I WAS HAVING SOME TECHNICAL TROUBLES HERE.

I ACTUALLY DON'T WANT A POINT OF DISCUSSION. I WANTED TO BACK UP WHAT PAT AND CHRISTINE AND OTHERS HAVE SAID, BUT I'D LIKE TO GIVE IT A SLIGHTLY DIFFERENT PERSPECTIVE. AND THE PURPOSE OF MY SAYING THIS IS SIMPLY TO UNDERSCORE

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HOW IMPORTANT THIS IS TO PATIENTS. IT'S ONE THING TO TALK ABOUT GOOD SCIENCE, AND I THINK WE DO AN ADMIRABLE JOB OF BRINGING FORTH THE GREAT SCIENCE, BUT I'LL TELL YOU. ME PERSONALLY, I'M THE PARKINSON'S REPRESENTATIVE ON THE BOARD. I HAVE PARKINSON'S DISEASE MYSELF. AND TO HEAR THE ORGANIZATION AND THE DEDICATION AND THE PURPOSEFULNESS OF THIS GROUP AND HOW YOU'RE GOING ABOUT GATHERING THE INFORMATION YOU NEED TO IT TURN IT INTO SOMETHING THAT CAN BE A PRODUCT, I KNOW PRODUCTS ARE FAR DOWN THE STREAM. AND I THINK MOST PEOPLE RECOGNIZE THAT. BUT I JUST WANT YOU TO KNOW THAT FROM THE PATIENT'S POINT OF VIEW, FROM A PERSON WITH PARKINSON'S WHO I KNOW WITHIN THE NEXT 10, 20 YEARS I'M GOING TO DIE, THE NOTION THAT PARKINSON'S IS NOT LETHAL IS BULLSHIT. EXCUSE ME. BUT IT WARMS MY HEART TO LOOK AT THIS COMPUTER SCREEN AND SEE ALL THESE PEOPLE WHO GOT UP TODAY AND CARED ENOUGH TO SHOW UP AND PUT OUT. SO FOR THAT THANK YOU.

CHAIRMAN GOLDSTEIN: THANK YOU, DAVID. VERY NICE OF YOU. AND I ALSO AGREE WITH YOU, OF COURSE.

OTHER COMMENTS BEFORE WE GO TO PUBLIC COMMENT? LET'S SEE. WHO'S IN CHARGE OF THE PHONE LINE? LANA?

MS. MORALEZ: IF WE HAVE ANYBODY FROM THE PUBLIC THAT WOULD LIKE TO MAKE A COMMENT, JUST PRESS STAR NINE. NO PUBLIC COMMENT.

CHAIRMAN GOLDSTEIN: WE ARE CLEAR. SO WE'VE GOT A MOTION, SECONDED. DISCUSSION. I THINK WE ARE READY TO VOTE. LANA, CALL THE ROLL PLEASE.

MS. MORALEZ: HAIFAA ABDULHAQ.

DR. ABDULHAQ: YES.

MS. MORALEZ: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

MS. MORALEZ: MONICA CARSON.

DR. CARSON: YES.

MS. MORALEZ: MARK FISCHER-COLBRIE.

MR. FISCHER-COLBRIE: YES.

MS. MORALEZ: ELENA FLOWERS.

DR. FLOWERS: YES.

MS. MORALEZ: JUDY GASSON.

DR. GASSON: YES.

MS. MORALEZ: LARRY GOLDSTEIN.

CHAIRMAN GOLDSTEIN: YES.

MS. MORALEZ: DAVID HIGGINS.

DR. HIGGINS: YES TO BOTH.

MS. MORALEZ: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: YES.

MS. MORALEZ: PAT LEVITT.

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DR. LEVITT: YES.
MS. MORALEZ: CHRISTINE MIASKOWSKI.
DR. MIASKOWSKI: YES.
MS. MORALEZ: KARL WATSON.
DR. WATSON: YES.
MS. MORALEZ: KEITH YAMAMOTO.
DR. YAMAMOTO: YES.
MS. MORALEZ: SHLOMO MELMED.
OKAY.
CHAIRMAN GOLDSTEIN: ALL RIGHT. THANK YOU ALL FOR YOUR ATTENTION TO THIS IMPORTANT PROGRAM. WE WILL BE FOLLOWING UP AT SOME POINT WITH FURTHER REPORTS FROM THE TASK FORCE, WHICH IS NOW GOING TO TACKLE NEURONAL INJURY DISORDERS AND NEURODEGENERATIVE ORDERS, EACH AS A CLASS, AND WILL GIVE YOU AN UPDATE IN THE NEXT FEW MONTHS.
THE NEXT ITEM ON THE AGENDA IS THE PRIORITIZATION KICKOFF DISCUSSION. MARK FISCHER-COLBRIE, THAT'S YOU.
DR. FISCHER-COLBRIE: SORRY ABOUT THAT. THANK YOU VERY MUCH FOR THE OPPORTUNITY TO TALK ABOUT A GENERAL TOPIC, WHICH IS MEANT TO BE AN OPEN DISCUSSION AND IN SOME WAYS PIGGY-BACKS OFF OF THE ACTIVITIES AND PROCESS RELATED TO THE NEURO TASK FORCE, WHICH THE TEAM DID A TERRIFIC JOB ON. SO

THIS IS MEANT TO BE AN OPEN, GENERAL DISCUSSION. WITHIN THAT CONTEXT, I WOULD LIKE TO PROVIDE SOME CONTEXT, SOME BACKGROUND INFORMATION AS A QUICK WAY OF INTRODUCTION, WHILE I'M HOPEFULLY PULLING UP THE SCREEN HERE, IT'S A SITUATION WHERE JUST AN INTRODUCTION OF MYSELF. FOR THOSE OF YOU WHO DON'T KNOW ME, I'M THE TYPE 1 DIABETES PATIENT REPRESENTATIVE FOR CIRM AND OBVIOUSLY ON THE BOARD AND THE GRANTS WORKING COMMITTEE.

BUT WITH THAT IN MIND, JUST WANTED TO GIVE SOME CONTEXTUAL BACKGROUND INFORMATION AROUND DISCUSSION AROUND DISEASE AND DIAGNOSTIC AND PRIORITIZATION PROCESSES RELATED TO THINGS THAT WE MIGHT WANT TO CONSIDER AROUND CIRM MODELS. AND SO IF YOU'LL BEAR WITH ME A LITTLE BIT ON BACKGROUND, I THINK WE ARE QUITE FAMILIAR WITH THE FACT THAT CURE RESEARCH AND IN THIS CONTEXT, THIS TERMINOLOGY IS COVERING BOTH DIAGNOSTICS AND TOOLS, COVERING THE WHOLE REMIT OF WHAT CIRM DOES.

BUT CURE RESEARCH IS OBVIOUSLY VERY COMPLEX AND HIGHLY UNPREDICTABLE AS WE ALL KNOW. THIS IS A STRUGGLE THAT EVERYBODY IS DEALING WITH, WHETHER IT'S ACADEMICS RUNNING ALL THE WAY THROUGH PHARMA FIRMS. AND EVERYBODY HAS BEEN WORKING TOWARDS THE MODELS OF WHAT MAKES THE MOST SENSE FOR

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ACCELERATING THE DISCOVERY PROCESS.

THE INHERENT LIMITATIONS THAT ARE LEADING TO THE DIFFICULTIES AROUND COMING UP WITH PROVEN MODELS HAS TO DO WITH THE FACT THAT OBVIOUSLY THERE ARE MANY, MANY GAPS IN TERMS OF THE KNOWLEDGE AND THE SYSTEMS THAT ARE EMPLOYED IN ORDER TO ADVANCE DISEASE THERAPEUTICS. AND STARTING, OBVIOUSLY, WITH BASIC BIOLOGICAL KNOWLEDGE IS INCOMPLETE. I'M ACTUALLY QUITE AMAZED, FOR EXAMPLE, THAT INNATE IMMUNE SYSTEMS AND A CRITICAL FUNCTION OF TOTAL LIFE RECEPTORS WEREN'T DISCOVERED TILL THE LATE '90S, THAT BRAIN LYMPHATIC SYSTEM WASN'T DISCOVERED UNTIL THE LAST 24 MONTHS, THE UNDERSTANDING AND ACKNOWLEDGMENT OF THE ROLE OF THE MICROBIOME IS A RELATIVELY NEW MODALITY, IF YOU ARE LOOKING AT THAT.

IN TERMS OF THE OTHER AREAS OF GAPS, TOOLS IS A CRITICAL AREA, AND THAT IS EITHER LACKING OR DIDN'T EXIST. I THINK EVERYONE IS AWARE THAT CRISPR IS NEW AND IS REALLY ONLY STARTING TO HIT ITS PRIME HERE IN THE LAST HANDFUL OF YEARS.

THE OTHER NASCENT AREA IS ARTIFICIAL INTELLIGENCE. THAT'S GATHERING STEAM AND ACCELERATION AND IS A VERY PROMISING AREA OF BEING ABLE TO USE AS AN ACCELERANT TO THE DISCOVERY PROCESS, BUT AS OF THE MOMENT, THERE'S A LIMITED

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IMPACT AS TO HOW THAT'S BEEN PROSECUTED TO DATE.

THE OTHER HAS TO DO WITH THE FACT OF THE BOTTLENECK OF THE DUAL PHENOMENON. ANIMAL MODELS ARE BOTH LESS AND LESS PREDICTIVE OF THE IMPACT ON HUMANS. AND, IN ADDITION, WHILE THERE IS AN EXPANSION OF IN VITRO MODELS, THERE'S A TREMENDOUS GAP THERE IN TERMS OF THE QUALITY OF THOSE IN VITRO MODELS IN TERMS OF HOW THAT MIGHT PREDICT TOXICITY AND EFFICACY IN HUMANS.

FINALLY, THERE'S ALSO CONTINUING TO BE A VERY DISTURBING LACK OF REPRODUCIBILITY OF EXPERIMENTAL RESULTS BECAUSE OF INHERENT LIMITATIONS OF MANY EXPERIMENTS BEING DONE ANNUALLY AND ALSO THE RELATIVELY POOR DATA RECORDINGS THAT CAN OCCUR IN DIFFERENT ORGANIZATIONS.

AS WE ALSO KNOW, THERE'S RESEARCH AND FUNCTIONAL SILOS RELATED TO THAT. I THINK EVERYONE IS FAMILIAR WITH THE FACT THAT, FOR EXAMPLE, IN CANCER IT WASN'T UNTIL CAR-T CAME ALONG THAT THERE WAS INCREASED INVOLVEMENT BETWEEN IMMUNOLOGISTS AND OTHER CANCER SPECIALISTS. MORE BROADLY, IT'S A REFLECTION OF THE FACT THAT THERE ARE OPPORTUNITIES FOR MORE AND MORE INTERACTIONS ACROSS FUNCTIONAL SILOS AS WELL AS DISEASE SILOS.

THE OTHER BIG INFLUENCE HERE IS FUNDING

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MODELS ARE EXTREMELY UNCERTAIN. FOR ACADEMICS, BECAUSE OF LIMITATIONS ON NIH FUNDING, WE ARE AT ONE POINT ONLY 6 PERCENT OF RESEARCH PROPOSALS WERE GETTING APPROVED BY THE NIH. THAT'S A SITUATION WHERE RESEARCHERS MAY HAVE A TENDENCY TO DIAL BACK AGGRESSIVE, NOVEL CONCEPTS TO INCREASE FUNDING. SO YOU START DOING EXPERIMENTS THAT ARE MORE INCREMENTAL BREAKTHROUGH. THE OBVIOUS PROBLEM OF PEOPLE NOT GETTING THEIR FIRST NIH GRANT TILL THEIR MID-40S IS ACTUALLY CAUSING RESEARCHERS TO LEAVE THE FIELD. AND SO THE FUNDING MODEL SITUATION IS PROBLEMATIC.

THIS IS EXACERBATED BY THE SITUATION OF THE OPPORTUNITY FOR TERRIFIC IDEAS THAT HAVE BEEN DISCOVERED IN ACADEMIA TO ACTUALLY PROGRESS ALL THE WAY THROUGH TO POTENTIAL THERAPY. AND THIS WELL-KNOWN PHENOMENON OF THE MILLIONS TO TENS OF MILLIONS REQUIRED TO STEP THROUGH THIS PROCESS, THE VALLEY OF DEATH, AS TO HOW THAT'S GOING TO GET FUNDED. EVERYONE'S FAMILIAR WITH THAT APPROACH. AND, THEREFORE, IT ENDS UP BEING A HEAVY, HEAVY RELIANCE ON PRIORITIZATION FROM PHARMA COMPANIES THAT ARE SEEKING TO FIGURE OUT A WAY TO DEAL WITH THE PROBLEM OF $2.5 BILLION IN A 15-YEAR TIMELINE TO GET A THERAPY TO MARKET. THIS CAUSES A LOT OF PULLS

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AND SHIFTS AND CONSEQUENCES OF VERY PROMISING DRUG AND DISEASE THERAPIES THAT NEVER GET PROSECUTED FURTHER BECAUSE OF THE FACT THAT THEY HAVE GREAT PROMISE, BUT THEY'RE SHELVED FOR NONSCIENTIFIC AND OFTEN FOR FINANCIAL REASONS.

THAT'S A LITTLE BIT OF BACKGROUND. I THINK EVERYONE HERE IS FAMILIAR WITH THOSE ELEMENTS. I APOLOGIZE FOR RECAPPING THAT.

BUT THE SITUATION ON CIRM AND HOW THIS RELATES TO CIRM IS ALSO THEN IN THE CONTEXT OF A LITTLE BIT BACKGROUND THAT THERE ARE VERY WELL ESTABLISHED AND RESPECTED PROCESSES IN PLACE WITH CLEAR GUIDELINES AND RULES OF ENGAGEMENT FOR HOW TO EFFECT THE SPECIFIC GOALS OF PROP 71 AND PROP 14. THE STRATEGIC PLAN DOES AN OUTSTANDING JOB OF DELINEATING THE OVERALL CONTEXT OF THE MISSION FOR THE ORGANIZATION WITHIN THE FRAMEWORK OF THE FIVE PILLARS. THERE'S REALLY BEEN GREAT WORK AT DELINEATING DISC AND TRAN AND CLIN THAT COVER THREE OF THE AREAS THAT ARE ON THE RESEARCH FOCUS ELEMENT. AND THE TEAM'S DONE AN OUTSTANDING JOB AT THIS.

THAT PRIORITIZATION PROCESS, JUST FOR THE REMINDER FOR PEOPLE, HAS FLEXED OVER TIME. IN THE EARLY DAYS OF PROP 71, FUNDING REQUIRED A VERY, VERY HEAVY INFRASTRUCTURE INVESTMENT IN FACILITIES AND

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BUILDINGS. THERE WAS A SHIFT AS PROP 71 STARTED TO WIND DOWN TO FOCUS ON CLINICAL TRIALS. AND EVEN SEPARATELY, DUE TO COVID, FUNDING PRIORITIZATION AROUND COVID ACTIVITY. SO IT'S AN ELEMENT OF ACKNOWLEDGING THAT THERE CONTINUES TO BE FLEX IN HOW DECISIONS ARE MADE ABOUT PRIORITIZATION RELATED TO THE DEFINED, VERY WELL-DEFINED OUTLINES. THE TEAM'S DONE AN OUTSTANDING JOB OF DELINEATING THIS.

A LITTLE BIT OF BACKGROUND. OBVIOUSLY WE ALL KNOW ABOUT THE $1.5 BILLION. AND NOW THE QUESTION IS WHAT ARE OUR OPTIONS AND OPPORTUNITIES. OBVIOUSLY WITH THE NEURO TASK FORCE, WE'VE ALREADY, IN EFFECT, CREATED A SLIGHTLY DIFFERENT MECHANISM FOR WORKING ON APPROVALS AND HOW TO BE ABLE TO, IN FACT, TAKE A MORE PROACTIVE ROLE IN HOW WE LOOK AT THE PROGRAMS THAT WE REVIEW AND APPROVE. BUT IN GENERAL, CERTAINLY TO DATE THE CURRENT CIRM FUNDING MODEL RELIES ON INCOMING APPLICATIONS TO MAKE ALLOCATION DECISIONS, AND THAT NATURALLY CREATES LIMITATIONS.

WHAT THAT MEANS IS TYPICALLY APPLICATIONS ARE COMING IN FROM SINGLE FUNCTIONS OR SINGLE ORGANIZATIONS. SO THERE'S A REDUCED CAPABILITY OF DIRECTING AND MANAGING AREAS THAT MIGHT REQUIRE STRONGER CROSS-TEAM, CROSS-ORGANIZATION FUNCTION.

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IT'S VERY RELIANT ON THE INBOUND APPLICATIONS. I CAN PERSONALLY ATTEST TO THE FACT THAT EVEN TODAY PEOPLE ARE STILL NOT NECESSARILY AWARE OF THE STANDARD REMIT OF PROP 14 WITH CELL THERAPY AND OTHER MODIFICATION TO CELLS THAT CAN BE FUNDED. SOME PEOPLE ACTUALLY ALSO GAVE UP ON APPLYING TO CIRM FUNDING AS PROP 71 WAS WINDING DOWN BECAUSE OF THE FACT THAT FUNDING GRANTS WERE GETTING DIRECTED IN A DIFFERENT DIRECTION. AND SOME PEOPLE ARE ALSO, I WAS SURPRISED, NOT UP TO SPEED ON THE ALLOCATION OF THE $1.5 BILLION IN NEURO.

WHAT THAT MEANS IS THERE'S A UNIVERSE OF APPLICATIONS AND RESEARCHERS THAT ARE NOT EVEN THINKING ABOUT SENDING THEIR APPLICATIONS IN. SO IT'S NOT AS IF THE APPLICATION PROCESS TODAY REPRESENTS THE ENTIRE UNIVERSE OF WHAT MIGHT BE POSSIBLE RELATED TO EVALUATE WITHIN THAT OR A MORE REACTIVE MODE.

SORRY FOR THE LONG PREAMBLE, BUT I WOULD LIKE TO STIMULATE A DISCUSSION FOR FOLKS AND REALLY START TO USE THIS AS A MECHANISM FOR AN ONGOING SET OF MEETINGS TO HAVE DISCUSSIONS AROUND WHAT ARE POSSIBILITIES. AND THAT MIGHT BE, HEY, SHOULD WE LOOK AT DIFFERENT APPROACHES TO ACHIEVING THE MISSION? SHOULD CIRM BE A SPARKPLUG AND AN

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INSTIGATOR, FORMING CONSORTIA. WE'RE IN A WAY SEEING A LITTLE BIT OF THAT WITH NEUROPSYCHIATRIC ACTIVITY. THIS IS SOMETHING THAT WE MIGHT WANT TO CONSIDER EXPANDING. IF SO, HOW DO YOU PICK A DISEASE AREA AND FOCUS AREA? AND THOSE KINDS OF THINGS REQUIRE SIGNIFICANT STAFF INVESTMENT OF TIME AND RESOURCES TO REALLY PROPERLY SUPPORT. IF, IN FACT, THERE IS A DESIRE TO DO SOMETHING LIKE THIS, THEN HOW DO YOU SUPPORT THOSE EFFORTS?

SHOULD CIRM REALLY TRY TO WORK EVEN FURTHER ON LEVERAGE? AND CIRM ALREADY DOES THIS WITH THE REQUIREMENTS OF ADDING ORGANIZATIONS BEING ABLE TO PROVIDE ADDITIONAL FUNDING AND OTHER ELEMENTS. BUT ARE THERE OTHER ASPECTS OF LEVERAGE THAT PEOPLE MIGHT CONSIDER? DO WE TAKE AN APPROACH OF, HEY, WE'D LIKE TO USE THE NORTH STAR. SOMETHING LIKE, HEY, WE WANT TO DO THE MOST GOOD FOR THE MOST PEOPLE IN THE SHORTEST AMOUNT OF TIME; I.E., FOCUS HEAVILY ON CLINICAL TRIALS AND FOCUS HEAVILY ON BROADER NUMBERS OF PEOPLE. YOU CAN GET A LITTLE BIT OF A FLAVOR OF THAT LOOKING AT THE SOCIOECONOMIC DATA AROUND HEALTH IMPACT, FOR EXAMPLE, THAT POINTS A LITTLE BIT IN THAT DIRECTION THAT WE DID WITH THE NEURO WORK.

THE OTHER ONE IS DO WE FOCUS IN ON FUNDING

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CRITICAL GAPS? AND SOMETIMES THESE ARE EXTREMELY NONSEXY GAPS, AND THEY'RE GAPS THAT ARE ELEMENTS THAT DON'T GET FUNDING FROM OTHER ELEMENTS. AND THIS REQUIRES, THEN, CONDITIONS LIKE ON THE NEURO, THE GAP IS TRYING TO BE FILLED FOR, HEY, LET'S ENCOURAGE PEOPLE TO COME IN WITH A DISCOVERY ON VERY KEY AND ESSENTIAL PROCESSES THAT WITHIN THE BRAIN CONTEXT ARE CURRENTLY MISSING. AND THAT'S A CRITICAL GAP THAT COULD BE EXPANDED INTO OTHER DISEASE AREAS EFFECTIVELY.

OR IS IT A SITUATION OF, HEY, YOU REALLY WANT TO INCREASE A PORTFOLIO ALLOCATION TO KEY TOOLS DEVELOPMENT AND FOCUS IN ON THAT? SO THAT GETS BACK TO THE SITUATION OF THAT DEARTH OF IN VIVO ANIMAL MODELING BEING VERY INEFFECTIVE IN DIFFERENT AREAS.

ANOTHER SET OF LEVERAGE POINTS IS DO WE LOOK AT MORE FORMAL TIE-INS SO WITH DIFFERENT ORGANIZATIONS, NON-PROFITS, THE NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES. THIS DOES NOT MEAN THAT WE'RE NOT CURRENTLY DOING THIS. THIS HAS TO DO WITH A QUESTION IS THERE PERHAPS WITHIN A CONSORTIA ELEMENT OR SOME TARGET THAT WE GO AFTER THAT WE DRAW PEOPLE IN ON A MORE FORMAL BASIS.

DO WE LOOK AT HOW WE MIGHT BE ABLE TO ACCELERATE AND ENCOURAGE NASCENT AI INTEGRATION OF

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THE DRUG DEVELOPMENT PROCESS AS A FURTHER ACCELERANT? DO WE LOOK AT FUNDING WHERE A CERTAIN MECHANISM OF ACTION OF DISEASE, EVEN THOUGH IT MIGHT BE FOR A RARE DISEASE, COULD, IN FACT, THEN BE APPLIED TO A POSSIBILITY OF MANY DISEASES. SO WE ARE LOOKING FOR LEVERAGE WITHIN THOSE CONTEXTS.

SO THAT'S A BIT OF BACKGROUND. THAT'S ENOUGH OF ME TALKING AND WOULD LOVE TO GET FEEDBACK AND RESPONSE TO THE SET OF ACTIVITY HERE TO HAVE A LITTLE BIT OF DISCUSSION AND THEN OBVIOUSLY START TO ASK CONSIDERATION ABOUT OF HOW WE MIGHT FRAME THE NEXT STEPS FOR FUTURE DISCUSSION POINTS. SO WITH THAT, I'D OPEN UP TO QUESTIONS AND COMMENTS.

CHAIRMAN GOLDSTEIN: COMMITTEE MEMBERS PLEASE.

DR. LEVITT: I'LL START.

CHAIRMAN GOLDSTEIN: THANK YOU, PAT.

DR. LEVITT: MY FIRST COMMENT IS WOW BECAUSE YOU TOUCHED UPON SO MANY PRESSURE POINTS IN UNDERSTANDING HOW WE MOVE OUT OF OUR WORLD OF INCREMENTAL ADVANCEMENT IN BIOMEDICAL SCIENCES AND RESEARCH. AND THAT'S SORT OF WHERE WE'VE BEEN SINCE THE NIH WAS INSTITUTED IN THE '50S. THEY HAVEN'T CHANGED THEIR MODEL VERY MUCH, WHICH IS ONE OF THE MAJOR PROBLEMS BECAUSE THE WAY SCIENCE IS DONE HAS

CHANGED DRAMATICALLY. AND THEY REALLY HAVE NOT CHANGED THEIR MODEL.

I WOULD SAY THE OTHER THING IS THAT -- AND A LARGE PART OF THE MODEL, MOST OF THE FUNDING GOES TO INCREMENTAL SCIENCE. AND THERE'S A LACK OF WILLINGNESS TO RECOGNIZE THAT INNOVATION -- ATTEMPTS AT INNOVATION MOSTLY FAIL. BUT IF YOU DON'T DO THAT, THEN YOU'LL NEVER SUCCEED. ANYBODY WHO'S READ ALL THE BOOKS ABOUT ALL THE INNOVATORS, THAT'S JUST PART OF THE FORMULA. AND THE MAJOR FUNDERS ARE UNWILLING TO TAKE THAT RISK. AND CERTAINLY BIG PHARMA IS UNWILLING TO TAKE THAT RISK, WHICH IS WHY IN THE AREA OF NEUROSCIENCE, WHICH I KNOW WELL, MANY LARGE PHARMA COMPANIES HAVE CLOSED THOSE PROGRAMS DOWN BECAUSE THEY'RE, AS I SAY, TOO RISKY. SO THERE'S SORT OF A PHILOSOPHICAL, CULTURAL ISSUE AROUND THIS.

THE OTHER THING I JUST WANT TO MENTION IS THAT SCIENCE HAS GOTTEN MUCH MORE EXPENSIVE IN A VERY SHORT PERIOD OF TIME. IT'S VERY EXPENSIVE TO DO SCIENCE NOW. THE NIH HAS NOT RESPONDED AT ALL. THE NSF HAS NOT RESPONDED AT ALL. PRIVATE FOUNDATIONS BY AND LARGE HAVE -- A FEW HAVE RESPONDED, BUT WITH VERY SMALL PROGRAMS. SO THAT'S SOMETHING TO CONTEMPLATE BECAUSE WHAT WE JUST HEARD

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IN TERMS OF THE NEURO CONCEPT FOR NEUROPSYCHIATRY, I VERY STRONGLY SUPPORT IT. IT SOUNDS LIKE A LOT OF MONEY; BUT WHEN YOU START ADDING UP THE COSTS, MUCH OF WHICH IS PERSONNEL AND THEN MATERIALS AND SUPPLIES THAT ARE SPECIALIZED FOR THIS KIND OF RESEARCH, THE MONEY EVAPORATES.

I THINK THE OTHER THING YOU TOUCHED UPON, MARK, IS SORT OF TRYING TO IDENTIFY THE KNOWLEDGE GAPS, OF WHICH THERE ARE MANY. AND THE ONES YOU HAD ON YOUR LIST ARE CERTAINLY NOT MAJOR KNOWLEDGE GAPS. THAT'S PROBABLY AN EASIER DISCUSSION TO HAVE THAN THESE OTHER ISSUES THAT YOU BROUGHT UP. BUT I JUST WANTED TO APPLAUD YOU FOR DOING A REALLY THOROUGH JOB AT BRINGING UP REALLY THE SIGNIFICANT PRESSURE POINTS. I'LL STOP THERE AND LET OTHERS COMMENT.

CHAIRMAN GOLDSTEIN: THANK YOU, PAT. OTHER THOUGHTS?

DR. MIASKOWSKI: MARK AND PAT, I AGREE WITH PAT'S COMMENTS. AND THE THINGS THAT APPEAL TO ME IS CAREFULLY THINKING ABOUT THE CONUNDRUM THAT PRECLINICAL RESEARCH DOESN'T TRANSLATE TO THE HUMAN. IT'S A REAL, REAL ISSUE FOR US TO THINK THROUGH.

I AGREE WITH PAT ABOUT THE NIH'S STRUCTURE AND PARTICULARLY WITH REGARD TO THE FACT THAT IT'S DISEASE FOCUSED. I THINK THERE ARE A NUMBER, AND I

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THINK YOU RAISED THIS IN YOUR SLIDE, MARK, WHAT I WOULD CALL UBIQUITOUS MECHANISMS. THAT IF WE BEGIN TO FIGURE THEM OUT, WE'LL CUT ACROSS A VARIETY OF HUMAN CONDITIONS, INFLAMMATION BEING ONE. ALL THE MAJOR CHRONIC CONDITIONS HAVE A BASIS, A PART OF THEIR BASIS IN THEIR PATHOPHYSIOLOGY IN INFLAMMATION.

I'M GOING TO OFFER ONE AREA WHICH IS AN AREA THAT'S NEAR AND DEAR TO MY HEART. WHEN LARRY PRESENTED THE CASE FOR NEUROPSYCHIATRIC CONDITIONS, THE ONE THAT CAME TO MIND FOR ME THAT HAS AS BIG CONUNDRUM IS CHRONIC PAIN. AND THIS IS ANOTHER AREA, AND I WAS CURIOUS IF THE NEUROSCIENCE TASK FORCE DID LOOK AT THIS BECAUSE IT'S A LITTLE PAROCHIAL BECAUSE IT'S SOMETHING I STUDY CLINICALLY. AND I DON'T KNOW HOW MANY OF YOU KNOW THAT ONE IN FIVE AMERICANS HAVE CHRONIC PAIN. IT COSTS THE UNITED STATES $150 BILLION A YEAR, AND IT DISPROPORTIONATELY AFFECTS PEOPLE FROM DIVERSE BACKGROUNDS.

SO I PERSONALLY WOULD LIKE US TO THINK ABOUT THESE UBIQUITOUS MECHANISMS THAT WE MIGHT BE ABLE TO GAIN SOME LEVERAGE IN AS WELL AS THINGS THAT COST THE AMERICAN PEOPLE A LOT, BOTH IN TERMS OF DOLLARS AS WELL AS IN TERMS OF THE BURDEN OF ILLNESS

ON THEM. I'M SURE THERE'S A NUMBER OF THEM THAT WE COULD LOOK AT.

CHAIRMAN GOLDSTEIN: THOSE ARE GREAT POINTS, PARTICULARLY THE ONE ABOUT PAIN. I JUST ADDED IT TO MY LIST OF THINGS FOR THE TASK FORCE TO THINK ABOUT.

DR. MIASKOWSKI: I'M NOT AN EXPERT ON THIS, STEM CELL OR GENETICS. I DID A QUICK SEARCH, AND THERE SEEMS TO BE DISCOVERY IN THIS SPACE. BUT I CAN TELL YOU THE BURDEN IN TERMS OF INDIVIDUALS, AND THE COMPLEXITY OF CHRONIC PAIN IS COMPARABLE, I THINK, TO NEUROPSYCHIATRIC DISORDERS.

CHAIRMAN IMBASCIANI: AND THE LACK OF TRULY EFFECTIVE NONADDICTIVE DRUGS.

DR. MIASKOWSKI: YEAH.

AND THE OTHER THING I WANTED TO MENTION RELATED TO THAT, LARRY, IS THERE HAS NOT BEEN A NEW DRUG TO MANAGE CHRONIC PAIN SINCE VIOXX WAS REMOVED FROM THE MARKET IN 2004. SO WE'RE TALKING 20 YEARS. AND THE PHARMACEUTICAL INDUSTRY WILL NOT TOUCH THIS PROBLEM BECAUSE OF THE OPIOID EPIDEMIC. AND, AGAIN, THAT COULD LINK TO THE NEUROPSYCHIATRIC STUFF IN TERMS OF OPIOID USE DISORDERS.

CHAIRMAN GOLDSTEIN: IT'S A GREAT POINT. OTHER -- KEITH, GOOD. THANK YOU. I WAS GOING TO

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CALL ON YOU ANYWAY.

DR. YAMAMOTO: I JUST WANT TO UNDERSCORE A POINT THAT PAT MADE. I THINK THERE -- I HAVE TWO THINGS TO SAY ABOUT THE NIH THAT I THINK THAT CIRM ALREADY IS ON A PATHWAY TO ADDRESS. THE FIRST IS THAT IN THE ENDLESS FRONTIERS DOCUMENT THAT VANNEVAR BUSH WROTE IN 1945. HE WAS RESPONDING, BY THE WAY, TO AN INQUIRY FROM PRESIDENT ROOSEVELT THAT ASKED, YOU, DR. BUSH, WERE REALLY INSTRUMENTAL IN BRINGING A GOVERNMENT INTERFACE TO SCIENCE DURING THE WAR, WORLD WAR II. AND NOW THAT THAT WAR IS OVER, SHOULD THE FEDERAL GOVERNMENT CONTINUE ITS INTERFACE, EXTEND OR CONTINUE ITS INTERFACE WITH SCIENCE OR NOT? AND IF SO, WHAT SHOULD THAT INTERFACE LOOK LIKE?

AND WHAT THEN SCIENCE ENDLESS FRONTIER ESSAY SAID WAS THAT, YES, THE FEDERAL GOVERNMENT SHOULD CONTINUE TO INTERACT WITH SCIENTISTS, SHOULD CONTINUE TO SUPPORT SCIENCE, AND SPECIFICALLY IT SHOULD DO TWO THINGS. IT SHOULD SUPPORT BASIC DISCOVERY RESEARCH, FUNDAMENTAL RESEARCH, AND IT SHOULD SUPPORT THE TRAINING OF THE NEXT GENERATION OF SCIENTISTS. AFTER THAT, BUSH SAID, INDUSTRY WILL TAKE OVER. THE PRIVATE SECTOR WILL TAKE OVER. THEY WILL LOOK AT THESE DISCOVERIES AND SEE WAYS THAT

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THOSE DISCOVERIES COULD BE APPLIED IN WAYS THAT WILL INCREASE THE HEALTH AND WELL-BEING OF THE AMERICAN PEOPLE.

AND IF THAT WAS EVER TRUE, IT IS DEFINITELY NOT TRUE NOW. AND THAT WAS ONE OF THE POINTS THAT PAT WAS MAKING. AND CIRM ACTUALLY GOES A LONG WAY IN MOVING THROUGH THAT -- ADVANCING ON THAT PROBLEM THAT THE NIH HAS ACTUALLY STAYED AWAY FROM. AND THAT IS REALLY DEVELOPING APPLICATIONS OF DISCOVERIES. THE NIH IS THE GREATEST KNOWLEDGE DISCOVERY ENGINE IN THE BIOMEDICAL SCIENCES IN THE WORLD. THERE'S JUST NO DOUBT ABOUT THAT. YOU CAN LOOK AT ANY MEASURE YOU WANT IN TERMS OF SIGNIFICANT DISCOVERIES, NUMBERS OF PAPERS PUBLISHED, BLAH, BLAH, BLAH, AWARDS KNOWN AS NOBEL PRIZES UNDER NIH FUNDING, AND IT'S TERRIFIC. BUT MOVING FORWARD FROM THAT HAS NOT DONE WELL. SO SORT OF IN RESPECT TO THE MANDATE THAT THE VANNEVAR BUSH DOCUMENT SET.

AND THIS IS SOMETHING THAT I THINK THAT CIRM TAKES A DIRECT SHOT AT WITH ITS MULTIPRONGED APPROACH OF DISCOVERY, TRANSLATION, AND CLINICAL AND MOVING THROUGH TO CLINICAL TRIALS AND BEGINNING TO DERISK SOME OF THE STUFF THAT INDUSTRY WON'T TOUCH FOR VARIOUS REASONS THAT WE ALL KNOW.

SO THAT'S GOOD. AND THE QUESTION IS

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WHETHER THAT CAN BE EXTENDED IN SOME WAY TO BE ABLE TO REALLY HAVE A STRONG STRATEGY OF FORMING PARTNERSHIPS WITH THE PRIVATE SECTOR THAT ACTUALLY GO BEYOND SUPPORTING CLINICAL TRIALS THAT THEY MIGHT NOT SUPPORT OR AT LEAST PUTTING ENOUGH SUPPORT BEHIND THEM THAT THE TRIALS CAN GET DONE AND WHERE CAN IT EXTEND FURTHER. THAT'S POINT 1.

POINT 2 PAT DIRECTLY ADDRESSED, AND THAT IS THE INCREMENTALISM OF NIH RESEARCH AND ITS FAILURE TO REALLY TAKE BIG RISKS THAT CAN ACTUALLY HAVE VERY BIG PAYOFFS, KNOWING THAT MANY OF THOSE RISKS, BY DEFINITION, ARE GOING TO LEAD TO FAILURE. IT'S A TREMENDOUSLY RISK AVERSE AGENCY, AND THAT LEADS TO REALLY SPENDING A LOT OF THAT BUDGET, OVER $45 BILLION NOW, ON QUITE LINEAR PEDESTRIAN RESEARCH. WE ALL WRITE THE GRANTS IN THAT WAY BECAUSE WE KNOW THAT'S THE ONLY WAY THEY'RE GOING TO GET FUNDED. BUT I THINK THAT CIRM HAS THE OPPORTUNITY TO REALLY FOCUS HARD ON GOING FOR RISKY PROJECTS, BECOMING KNOWN AS AN AGENCY THAT'S LOOKING FOR THAT.

I RUN A SMALL FUNDING PROGRAM AT UCSF IN BASIC SCIENCE. I'VE RUN IT FOR 25 YEARS. AND FOR THE FIRST SEVEN OR EIGHT YEARS IN OUR CALL FOR PROPOSALS WE ACTUALLY HAD IN THERE THAT SAID WE ARE

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ONLY LOOKING FOR GRANT PROPOSALS THAT THE NIH WILL LAUGH OUT OF THE ROOM. I WAS ENCOURAGED TO DROP THAT LANGUAGE AFTER A FEW YEARS UNFORTUNATELY, BUT THAT IS WHAT WE'RE LOOKING FOR. AND PEOPLE GOT TO KNOW THAT. AND THE $7 MILLION A YEAR, WHICH IS NOT MUCH OF OUR, IT'S 1 PERCENT OR HALF A PERCENT OF OUR BASIC RESEARCH REVENUE IS REGARDED AS THE MOST VALUABLE MONEY THAT UCSF RESEARCHERS CAN GET, WRITING TWO PAGES AND GETTING A COUPLE HUNDRED THOUSAND DOLLARS TO TRY OUT A BOLD AND CRAZY IDEA.

AND I HOPE THAT -- I WOULD LIKE IF CIRM GOT TO BE REALLY KNOWN FOR THAT, THAT THAT'S WHAT THEY'RE LOOKING FOR. IF YOU'VE GOT AN IDEA THAT'S A GOOD NIH GRANT, WRITE AN NIH GRANT. IF YOU HAVE AN IDEA THAT THEY'LL LAUGH OUT OF THE ROOM, WRITE A CIRM GRANT. I THINK THAT KIND OF FOCUS MIGHT BE SOMETHING THAT, IN A GENERAL WAY, NO MATTER WHAT AREAS WE FOCUS ON, COULD REALLY HAVE A BIG IMPACT.

CHAIRMAN GOLDSTEIN: THANK YOU, KEITH. I WONDER IF I MIGHT FOLLOW UP WITH YOU ON ONE POINT. AS MANY OF THE FOLKS ON THIS CALL KNOW, THERE'S LEGISLATION CALLED BAYH-DOLE, WHICH ESTABLISHES A PROCESS THAT WAS HOPED TO REALLY EXPAND INVOLVEMENT OF INDUSTRY IN THE DEVELOPMENT OF THERAPIES BASED ON DISCOVERIES MADE IN ACADEMIA.

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I GUESS THE QUESTION FOR YOU, KEITH, IS DO YOU THINK THE TIME HAS COME TO DO SOMETHING ABOUT IT? CHANGE BAYH-DOLE? SCRAP BAYH-DOLE? REPLACE IT WITH AN ENTIRELY NEW PROCESS? WHAT DO YOU THINK?

DR. YAMAMOTO: ABSOLUTELY. I THINK THAT IN ONE SENSE, THE TIME HAS COME TO DO SOMETHING ABOUT IT. POLITICALLY IT'S NOT A GOOD TIME. IT DOESN'T MEAN THAT IT WOULDN'T BE A GOOD IDEA TO START WORKING ON IT. AND THERE ARE MEMBERS OF CONGRESS THAT AGREE WITH THAT AND I THINK WOULD BE VERY WILLING TO SIT DOWN AND START LOOKING AT HOW BAYH-DOLE COULD BE MODIFIED OR SCRAPPED, AS YOU SAID, TO ACTUALLY FACILITATE.

I THINK WHAT THEY STARTED OUT WANTING TO DO, BUT OBVIOUSLY IT HASN'T SERVED. AND SO I THINK THAT WOULD BE A FINE THING FOR PEOPLE THAT ARE WORKING IN SCIENCE POLICY, AS I DO, TO BEGIN TO PUT SOME FOCUS ON IT.

CHAIRMAN GOLDSTEIN: THANK YOU.

MARIA BONNEVILLE HAD HER HAND UP THERE FOR A WHILE BUT THEN TOOK IT DOWN. I'M GOING TO PUT HER ON THE SPOT HERE.

VICE CHAIR BONNEVILLE: THANKS, LARRY. A COUPLE OF THINGS. I THINK, DEPENDING ON WHERE WE END UP TODAY, I THINK A VERY CLEAR ASK OF THE

INTERNAL TEAM OF INFORMATION THAT YOU WOULD LIKE THEM TO BRING BACK TO THE BOARD SO THAT WE CAN CONTINUE OUR CONVERSATIONS AND START TO MAKE SOME DECISIONS I THINK IS REALLY IMPORTANT. SO AS CLEAR AS WE CAN BE SO THAT MARIA CAN DIRECT THE INTERNAL TEAM AS TO INFORMATION TO BRING BACK.

THE SECOND WOULD BE IF WE DID NOTHING, WHERE WOULD WE BE? LIKE IF WE JUST CONTINUE TO FUND THE WAY WE HAVE BEEN FUNDING, WHAT DOES THAT LOOK LIKE? WHAT DOES OUR PORTFOLIO LOOK LIKE?

I THINK WE'VE TALKED ABOUT DIFFERENT SCENARIOS BEFORE, BUT WHAT ARE THOSE SCENARIOS BECAUSE I THINK, WITHOUT KNOWING THAT, I'M NOT SURE THAT WE CAN COME TO A LOT OF DECISIONS ABOUT WHAT MAY OR MAY NOT BE MISSING OR WHAT DIRECTION WE WANT TO GO.

THE OTHER THING IS RIGHT NOW THE BOARD DOES RIGHT NOW HAVE THE ABILITY TO SAY NO TO APPLICATIONS THAT HAVE GONE THROUGH THE PROCESS, THAT HAVE RECEIVED FUNDING -- RECOMMENDATIONS TO FUND, BUT WE MAY NOT -- THEY MAY NOT BE NECESSARY FOR OUR PORTFOLIO CURRENTLY. THOSE ARE HARD DECISIONS THAT THE BOARD WOULD HAVE TO MAKE IN PUBLIC, BUT THAT IS AN OPTION THAT THE BOARD HAS. JUST AS WE HAVE THE OPTION IF THERE'S SOMETHING THAT

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RECEIVED PERHAPS AN 83, NOT AN 85, BUT FITS WITHIN OUR PORTFOLIO, WE CHOOSE TO FUND THOSE SOMETIMES AS WELL.

SO WE DO HAVE A MECHANISM BY WHICH WE CAN START TO NARROW PORTFOLIO IF THAT'S SOMETHING THAT WE CHOOSE IS IMPORTANT TO DO.

CHAIRMAN GOLDSTEIN: THANK YOU, MARIA. VITO.

CHAIRMAN IMBASCIANI: HI, EVERYONE. LET ME SPEAK FROM A THIRTY THOUSAND POINT OF VIEW. I HAVE THREE COMMENTS I WANT TO MAKE. NO. 1 TO MARK.

MARK, YOU DID SUCH A BROAD -- YOUR PRESENTATION WAS SO WONDERFUL IN ITS BREADTH AND DEPTH THAT I HESITATE TO COMMENT, EVEN TO COMPLIMENT YOU ON IT SORT OF EXTEMPORANEOUSLY BECAUSE I THINK THE WORK YOU PUT INTO THAT DESERVES CONSIDERED RESPONSE. BUT, ANYWAY, HATS OFF.

AND I WANT TO AMPLIFY SOME OF THE THINGS YOU SAID AND DRAW FROM THE COMMENTS THAT PAT AND CHRISTINE MADE FOLLOWING. BEFORE I DO THAT, I WANT TO THANK KEITH. I THINK, KEITH, YOU CONTINUE TO GIVE US LESSONS FROM HISTORY. AFTER A YEAR ON THE BOARD WITH YOU, I THINK I'M GOING TO ASK FOR A MASTER'S IN HISTORY THANKS TO YOU. YOUR COMMENTS WERE GERMANE, AND I LOVE THE KICK THEM OUT OF THE

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ROOM THING.

AND, MARK, IF I CAN MARRY UP KEITH'S LAST COMMENT WITH ONE OF YOUR BULLET POINTS ABOUT CAN WE THE MOST QUICKLY FOR THE MOST NUMBER OF PEOPLE. AND HERE'S WHERE I'M COMING IN AT THE 3,000 LEVEL. I HAVEN'T SPOKEN TO OUR PRESIDENT YET OR TO OTHER MEMBERS OF THE LEADERSHIP TEAM. BUT I'M WONDERING, I WANT TO ENCOURAGE THIS TASK FORCE, THIS SUBCOMMITTEE, EXCUSE ME, TO CONSIDER WHETHER, AS WE START OUR THIRD DECADE NEXT YEAR AT CIRM, WHETHER WE CAN NOW, AND I HAVE TO BOW TO CONSIDERED SCIENTIFIC OPINION, IS THE CAR-T, FOR EXAMPLE, AND I'M JUST GIVING EXAMPLES, HAS ENOUGH RESEARCH BEEN DONE ACROSS THE BOARD THAT THAT LEVEL OF RESEARCH MAY NOT NEED AS MUCH SUPPORT? HAS THE RESEARCH INTO SMALL DRUGS, FOR EXAMPLE, ARE ENOUGH OTHER PEOPLE OUTSIDE CIRM ENGAGED IN THAT, THAT WE CAN PULL BACK A LITTLE BIT FROM THERE? WHY? TO FOCUS, TO MEET THE CHALLENGE OF YOUR BULLET POINT.

BECAUSE I'M ALSO CONCERNED AS BOARD CHAIR, I SEE NUMBERS OF HOW LONG AT OUR PRESENT BURN RATE, HOW LONG WILL OUR MONEY LAST? SOME PEOPLE GIVE ME AN ESTIMATE OF TEN YEARS. OTHER PEOPLE MAY SAY ONLY SEVEN YEARS. SEVEN YEARS SCARES ME. IT REALLY DOES. TEN YEARS IS THE MINIMUM. BUT MAYBE -- I

KNOW OUR MISSION SAYS ACCELERATE, AND I KNOW I'M ALL OVER THE MAP WITH THIS COMMENT, BUT I WANT TO COME UP WITH SOMETHING THAT'S GOT IMPACT INTO REAL PEOPLE'S LIVES IN THE TIME, IN THE LIFE SPAN THAT CIRM HAS WITHOUT BANKING ON YET A THIRD RENEWAL.

SO I'M GOING TO ENCOURAGE THIS SUBCOMMITTEE TO CONTINUE THINKING ABOUT IT AND MAYBE EVEN GO SO FAR, BE SO BOLD, THROW THEM OUT OF THE ROOM, TELL THE BOARD TO CONSIDER CLOSING THE DOOR TO CERTAIN APPLICATIONS. NOW, THAT MAY BE PRETTY BOLD FOR THIS. DID I GO TOO FAR?

DR. FISCHER-COLBRIE: GREAT COMMENTS FIRST OF ALL. SECOND, CLOSE THE DOOR TO APPLICATIONS, BUT ALSO BE THAT MAGNET TO DRAW IN NEW ONES THAT WE OTHERWISE MIGHT MISS KIND OF THING.

I THINK RELATED TO YOUR COMMENTS -- BY THE WAY, THANK YOU VERY MUCH FOR VERY KIND WORDS. I CONTINUE TO BE INCREDIBLY IMPRESSED WITH, EXTREMELY IMPRESSED WITH THE CIRM STAFF. AND THEY'VE GIVEN COLLECTIVELY A LOT OF THOUGHT TO THIS IN THE STRATEGIC PLANNING PROCESS AND IN OTHER ELEMENTS. AND THERE WOULD NATURALLY BE A TREMENDOUS MARRIAGE ON ANY SORT OF SUBCOMMITTEE OR DISCUSSION WORK THAT WOULD WANT TO WORK HAND IN HAND WITH THE STAFF. IN FACT, WOULD LOVE TO GET ANY COMMENTS ON MARIA AT

THIS JUNCTURE AS WELL.

DR. MILLAN: THANK YOU VERY MUCH. AND I ALSO ECHO THE REMARKS THAT THAT WAS AN EXCELLENT STARTING POINT FOR THIS DISCUSSION, YOUR PRESENTATION.

I THINK THAT IN ADDITION TO CONSIDERING WHERE WE SHOULD IDENTIFY AREAS WHERE WE MAYBE REDIRECT FOCUS FROM AND INTO, I THINK, MOST IMPORTANTLY IS WHERE ARE THE KEY OPPORTUNITIES.

YOU BROUGHT UP IN ONE OF THE SLIDES SOME PARTNERSHIP OPPORTUNITIES BECAUSE THERE IS A CONSIDERABLE AMOUNT OF PROGRESS BEING MADE ACROSS MULTIDISCIPLINARY AS WELL AS MULTI -- INCORPORATING TECHNOLOGIES AND VARIOUS STAKEHOLDERS AND VARIOUS AREAS. AND HAS BEEN CIRM PRESENTED THE OPPORTUNITY TO PARTNER WITH SOME OF THESE PROGRAMS. SO HAVING THE AVENUE FOR A DELIBERATE PARTNERSHIP THAT ALLOWS FOR THAT WOULD BE REALLY SOMETHING THAT'S WORTHWHILE CONSIDERING BECAUSE WE DON'T HAVE TO BUILD EVERYTHING FROM SCRATCH. THERE'S A LOT OF EXTREMELY BRIGHT MINDS OUT THERE AND A LOT OF INVESTMENT THAT'S BEEN PUT IN AND IT'S PRESENTED TO US.

BUT CURRENTLY WHAT WE HAVE IS THE OPPORTUNITY TO HAVE THOSE PARTNERSHIPS IF IT FALLS INTO OUR CURRENT PILLAR STRUCTURE, INTO OUR CURRENT

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STRUCTURE OF HOW WE FUND PROGRAMS ACROSS THE PILLARS, WHICH WORKS VERY WELL IN TERMS OF AN ENGINE TO GENERATE WHAT IT HAS. BUT IN TERMS OF CRAFTING STRATEGICS IN SPECIFIED AREAS WHERE YOU CAN PROMOTE MULTIDISCIPLINARY, I THINK, PUTTING PARAMETERS AROUND PRIORITIES AS WELL AS STRUCTURE OF THOSE TYPES OF PARTNERSHIPS, I THINK, WILL BE REALLY ENABLING AND COULD REALLY ACCELERATE BY USING THAT FORMAT.

TO MARIA'S POINT OF PLEASE LET US KNOW WHAT WE CAN BRING FORWARD TO ASSIST IN THIS DISCUSSION, THE MEMBERS OF THE LEADERSHIP TEAM AND MEMBERS OF THE TEAM REALLY HAVE A LOT OF REALLY GREAT IDEAS THAT IN SOME FORMAT WOULD LOVE TO SHARE WITH THE SCIENCE SUBCOMMITTEE FOR CONSIDERATION AS YOU GO THROUGH THIS AS WELL.

SO FOR NOW THAT'S ALL I HAVE, AND THANK YOU FOR THE OPPORTUNITY TO WEIGH IN.

CHAIRMAN GOLDSTEIN: THANK YOU, MARIA. MONICA.

DR. CARSON: JUST VERY IMPRESSED BY THIS WHOLE DISCUSSION FIRST AND FOREMOST BY THE PRESENTATION AND ALL THE CONTEXT. PLEASE FORGIVE ANY NAIVETE I HAVE FOR DISCUSSIONS THAT YOU MAY ALREADY HAVE HAD. BUT WHAT I WAS JUST STRUCK BY IS

BOTH AN ALMOST A VERY IDENTICAL CONVERSATION THAT WAS HAD ON A MUCH SMALLER DOLLAR LEVEL BY THE NATIONAL MULTIPLE SCLEROSIS SOCIETY SOME YEARS AGO WHEN THEY LAUNCHED THEIR FAST FORWARD PROGRAM, AND I SERVED ON THOSE STUDIES SECTIONS.

AND LISTENING TO ALL OF THESE THINGS IN ADDITION TO ALL THE THINGS YOU'RE SAYING, LOOKING AT HOW OTHER FUNDING AGENCIES OUTSIDE OF NIH HAVE TRIED TO GET THAT INNOVATIVE, THAT LAUGHS OUT OF THE ROOM, BUT ALSO THE PRAGMATISM OF IT. AND ONE OF THE THINGS WITH FAST FORWARD WAS THAT THE PARTNERS HAD TO COME SHOWING THEY HAD PROTECTED IP OR IP THAT COULD BE RAPIDLY PROTECTED BECAUSE IF IT CAN'T BE, YOU'RE NOT GETTING THAT TO THERAPIES AS FAST AS POSSIBLE AND ACTUALLY WHY THIS COULDN'T BE FUNDED BY VENTURE CAPITAL BY THESE OTHER KINDS OF STUFF. IT HAD A LITTLE BIT OF A HIGH RISK, HIGH REWARD THING THAT THE ARPA-H AND SOME OF THE OTHER OLDER NIH MECHANISMS TRIED TO DO.

SO ONE OF THE THINGS I WAS CURIOUS ABOUT IS HAVE THERE BEEN AN INVESTIGATION OF OTHER FUNDING AGENCIES IF THEY'VE DONE IT SMALLER OR EVEN WHAT ARPA-H IS TRYING TO DO AND WE DO IT HERE SMALLER THAT CAN BE APPLIED TO ACTUALLY BRIDGE WHATEVER EVERYBODY CALLS THAT VALLEY OF DEATH BETWEEN THE

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FINDINGS, BIOMEDICAL FINDINGS, AND THE ACTUAL THERAPIES. SO THANK YOU. I JUST WAS VERY IMPRESSED BY THE DISCUSSION.

CHAIRMAN GOLDSTEIN: GOOD POINT. I MIGHT POINT OUT THAT CIRM HAS DONE WHAT I THINK IS ACTUALLY A VERY GOOD JOB OF TRYING TO BRIDGE THE VALLEY OF DEATH BY FUNDING IN THE TRANSLATIONAL SPACE PRIOR TO ANY INDUSTRY INVOLVEMENT. AND A CONVERSATION THAT I'VE HAD WITH SOME OF THE FOLKS ON THIS CALL, BUT NOT EVERYBODY, IS DO WE ALWAYS REALLY NEED INDUSTRY TO DEVELOP A THERAPY? ONE OF THE PROBLEMS WITH RELYING ON INDUSTRY AND VENTURE CAPITAL IS THAT YOU CAN HAVE A GREAT IDEA; BUT IF IT'S NOT PROTECTABLE WITH A PATENT SUITE, IT'S GOING TO BE REALLY HARD TO GET IT DEVELOPED, BUT IT MIGHT BE A TERRIFIC IDEA OR THERAPY, OR, FOR EXAMPLE, REPURPOSING ALREADY APPROVED FDA DRUGS.

IF YOU FIND THAT AN EXISTING DRUG HAS A REALLY GREAT EFFECT IN A STEM CELL MODEL OF SOME DISEASE, BUT IT'S BEEN ON THE MARKET FOREVER, IF YOU RELY ON INDUSTRY TO DO IT, YOU HAVE NO PATENT PROTECTION AND YOU CAN'T GET THEM INTERESTED. I WONDER WHETHER THIS IS A PLACE WHERE CIRM OR CIRM IN PARTNERSHIP WITH OTHER AGENCIES THAT ARE PERHAPS DISEASE SPECIFIC COULD FUND THOSE LAST FEW STEPS IN

SOME CASES TO BRING A THERAPY TO APPLICATION THROUGH DEVELOPMENT IN AN ACADEMIC HEALTH CENTER AS OPPOSED VIA INDUSTRY. JUST A COMMENT.

CHRISTINE.

DR. MIASKOWSKI: I WANTED TO DISCUSS A LITTLE FURTHER THIS NOTION OF FUNDING HIGH RISK, HIGH REWARD PROJECTS. AND I'M GOING TO OFFER AS AN EXAMPLE, I SIT ON THE SCIENTIFIC BOARD FOR THE AMERICAN CANCER SOCIETY, AND I'VE BEEN AN AMERICAN CANCER SOCIETY PROFESSOR. AND ONE OF THE THINGS THAT THEY LAUD QUITE BROADLY IS THE FACT THAT THEIR PORTFOLIO OFTEN FUNDS HIGH RISK, HIGH REWARD PROPOSALS, AND THOSE HAVE PRODUCED 25 NOBEL LAUREATES.

CURRENTLY, IN TERMS OF MY WORK ON THAT BOARD, THEY ARE FRAMING THEIR PORTFOLIO TO BE MORE DIRECTED IN TERMS OF WHAT I WOULD CALL TARGETED OPPORTUNITIES IN THE SCIENTIFIC SPACE NEEDED FOR CANCER RESEARCH. SO THEY'VE DONE -- THE STAFF HAS DONE SOME DELIBERATE WORK TRYING TO IDENTIFY GAPS, AND THEN THEY'RE DOING REQUESTS FOR PROPOSALS BASED ON THOSE IDENTIFIED GAPS, BOTH ON THE TRAINING SIDE IN TERMS OF JUNIOR INVESTIGATORS OR YOUNG INVESTIGATORS AS WELL AS IN TERMS OF THE GRANT PORTFOLIO. AND THEY STILL HAVE THEIR GENERIC CALL,

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BUT THEY'RE PUTTING SET-ASIDE MONIES FOR THAT. SO THAT MIGHT BE A MODEL, I THINK, WE'VE TALKED ABOUT AND COULD CONSIDER IN OUR WORK.

CHAIRMAN GOLDSTEIN: I'LL JUST NOTE THAT MY FIRST EVER GRANT WAS FUNDED BY THE ACS AND LAUGHED OUT OF THE ROOM AT THE NIH.

DR. MIASKOWSKI: YEAH. IT'S A VERY INTERESTING ORGANIZATION IN TERMS OF HOW THEY DO THEIR PORTFOLIO.

CHAIRMAN GOLDSTEIN: YES. KEITH.

DR. YAMAMOTO: FIRST TO COMMENT ON YOUR POINT ABOUT WHETHER EVERYTHING TO AT THE END OF THE DAY BE SUPPORTED BY INDUSTRY. AND I THINK CLEARLY THE ANSWER IS NO. AND CIRM ALREADY IS IN THAT SPACE WITH THE SUPPORT IT'S GIVEN TO VARIOUS SCID PROJECTS. THE NOTABLE ONE THAT WE'RE ALL AWARE OF IS ORCHARD THERAPEUTICS AND WHAT HAPPENED TO THAT. AND I THINK THAT I'VE HAD GOOD CONVERSATION WITH MARIA ABOUT THIS. THIS IS AN EXAMPLE THAT I THINK CIRM SHOULD NOT SHY AWAY FROM. NOT ONLY THAT, WE SHOULD BE PROUD OF THE FACT THAT WE'VE CARRIED A PROJECT TO THE POINT WHERE THIS DILEMMA HAS JUST BLOWN UP IN A VERY PUBLIC WAY WHERE A COMPANY WAS WILLING TO TAKE ON A CERTAIN AMOUNT OF RISK UNTIL THEY REALLY BEGAN TO SEE THE DIMENSIONS OF IT AND

THEN JUST BALED AND LEFT THE INTELLECTUAL PROPERTY. I GUESS IT EVENTUALLY DID RETURN IT TO UCLA.

BUT THERE'S GOING TO BE A WHOLE RANGE OF DISEASES AND DISORDERS THAT CIRM COULD TAKE ON, LIKE THE SCID DISORDERS. THERE'S MORE THAN THE ONE THAT UCLA HAS TAKEN ON. THEY'RE SUPPORTING ONE FROM UCSF RIGHT NOW. AND WHERE THERE'S NOT GOING TO BE AN ENDPOINT THAT SAYS, ALL RIGHT, WE CARRIED THIS THROUGH THE PATHWAY AND NOW INDUSTRY CAN TAKE OVER. INSTEAD, IT'S GOING TO HAVE TO BE SOMETHING LIKE BEING ABLE TO CARRY FORWARD IN AN ACADEMIC MEDICAL CENTER SETTING OF SOME SORT THAT I THINK CAN DEFINITELY BE ARRANGED.

SO CERTAINLY AN AREA WHERE INDUSTRY IS REALLY RETICENT IS IN RARE DISEASES, VERY SMALL PATIENT GROUPS AND VERY RARE DISEASES LIKE SCID WHERE THERE'S ONLY A FEW PATIENTS A YEAR IN THE UNITED STATES FOR THE VARIOUS SPECIFIC SCID DISORDERS.

AND I THINK THAT CIRM, AS I SAID, SHOULD BE PROUD THAT THEY'VE CARRIED THE BALL TO REACH TO PUT A HEADLINE UNDER THESE KINDS OF PROBLEMS AND SHOULD BE THINKING HARD AND NEGOTIATING WITH ACADEMIC GROUPS AND OTHERS, NON-PROFITS, TO BE ABLE TO SAY, ALL RIGHT, NOW THAT WE'VE GOTTEN THROUGH

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THIS CLINICAL TRIAL AND INDUSTRY HAS REALLY SHOWN THAT IT'S NOT GOING TO CARRY THINGS FORWARD, WHAT DO WE DO AND WHAT CAN CIRM DO TO REALLY BE ABLE TO CREATE A SMOOTH PATHWAY FOR THESE THINGS THEN TO BE ABLE TO GO FORWARD AND BE ABLE TO MAKE USE OF THE TREATMENTS AND CURES THAT ARE GENERATED UNDER CIRM RESEARCH.

SO I THINK THAT'S -- RARE DISEASES IN GENERAL ARE A GREAT EXAMPLE OF THE KINDS OF THINGS THAT CIRM CAN DO, NOT JUST TO CROSS THE VALLEY OF DEATH, BUT THEN TO GO BEYOND IT TO ENSURE THAT THESE TREATMENTS ACTUALLY REACH PATIENTS.

CHAIRMAN GOLDSTEIN: INTERESTINGLY, THE SCID TECHNOLOGY HAS ALSO BEEN APPLIED TO CYSTINOSIS SUCCESSFULLY. AND ONE CAN SEE THAT THESE TECHNOLOGIES DEVELOPED IN RARE POPULATIONS CAN THEN EXPAND TO OTHER DISEASES AND I SUSPECT ULTIMATELY TO COMMON DISEASES.

MARIA MILLAN.

DR. MILLAN: SO I CAN'T RESIST A FOLLOW-ON TO THAT BECAUSE IN CONTINUATION TO THAT CONVERSATION YOU AND I HAD, KEITH, THERE HAVE BEEN MANY CONVERSATIONS WITH MANY MEMBERS OF THE BOARD AND OF THE INTERNAL TEAM. AND SO ONE OF THE THINGS, AGAIN IN RESPONSE TO WHAT THINGS WE CAN BRING TO THE

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COMMITTEE THAT MAY BE USEFUL, DR. ABLA CREASEY, WHO'S HEAD OF THE THERAPEUTICS DEVELOPMENT PROGRAM, HAS BEEN REALLY LOOKING AT DIFFERENT WAYS THROUGH OUR CURRENT FUNDING MECHANISM AS WELL AS OTHER AVENUES AND IS ARRANGING A WORKSHOP ACTUALLY IN NOVEMBER TO INFORM THAT. THE BOARD MEMBERS WILL BE INVITED TO THAT. BUT AT SOME POINT WE WELCOME THE OPPORTUNITY FOR DR. CREASEY AND OTHER MEMBERS OF THE TEAM TO BRING SOME IDEAS TO THE SUBCOMMITTEE TO CONSIDER IN THIS TOPIC, IN THIS AREA, AS WELL AS IN CONSIDERATION OF ALTERNATE MODELS.

AND THEN I'D LIKE TO ALSO SUPPORT THE NOTION THAT SUCCESS DOESN'T ALWAYS MEAN THAT IT'S SUCCESSFUL IN THE BIOPHARMA MODEL. I THINK THAT THERE MAY BE SUCCESSES THAT WE HAVE IN DELIVERING TRANSFORMATIVE AND CURATIVE TREATMENTS TO PATIENTS THAT ARE NOT DIRECTLY BROUGHT ALL THE WAY THROUGH BIOPHARMA. WE HAVE EXAMPLES OF THAT IN OTHER MODELS THAT ARE OUT THERE IN HEALTHCARE, SUCH AS ORGAN TRANSPLANTATION, WHICH IS THE AREA WHERE I STARTED, WHERE BIOPHARMA CERTAINLY IN TERMS OF IMMUNOSUPPRESSIVE MEDICINES, ET CETERA, IS VERY CRITICAL TO THE SUCCESS OF TRANSPLANTS, BUT THE DELIVERY AND THE ACTUAL IMPLEMENTATION IN THE HEALTHCARE IS WITHIN THE ACADEMIC AND HEALTHCARE

SETTING. THANK YOU.

CHAIRMAN GOLDSTEIN: MARIA, YOU BROUGHT UP THE POSSIBILITY THAT ABLA AND HER TEAM WOULD LIKE TO PRESENT TO THE SCIENCE SUBCOMMITTEE. DO YOU THINK THAT SHOULD BE BEFORE OR AFTER THIS PROPOSED NOVEMBER MEETING?

DR. MILLAN: IT'S REALLY -- I THINK -- I LIKE TO KIND OF HAVE A CONVERSATION INTERNALLY. I THINK THERE'S ALWAYS OPPORTUNITIES TO HAVE CONVERSATIONS ALONG THE WAY. CERTAINLY THE NOVEMBER MEETING WILL BE VERY INFORMATIVE, BOTH EXTERNAL STAKEHOLDERS AND OTHERS WHO ACTUALLY, WHEN YOU'RE TALKING ABOUT POTENTIAL PARTNERSHIPS AND OTHERS WHO HAVE BEEN DRIVING POTENTIAL SOLUTIONS, I THINK THAT WILL BE INFORMATIVE AND MAY BE HELPFUL TO BE INVOLVED IN THAT CONVERSATION AND THEN BRING IT BACK. AND THE SCIENCE SUBCOMMITTEE MAY FIND THAT TO BE USEFUL.

BUT I CAN ALSO CIRCLE BACK WITH ABLA AND LET YOU KNOW IF SHE THINKS THAT -- I DON'T KNOW THE SCHEDULE FOR THE SCIENCE SUBCOMMITTEE DISCUSSIONS. MARK, WE ARE ALWAYS AT YOUR DISPOSAL IF YOU'D LIKE FOR ABLA AND OTHER MEMBERS OF THE TEAM TO PRESENT EVEN A PREVIEW. THANK YOU.

CHAIRMAN GOLDSTEIN: MARIA, SO, YES, WHY

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DON'T YOU SPEAK TO ABLA AND THEN CIRCLE BACK WITH US. THIS IS AN IMPORTANT TOPIC. SO WE SHOULD WORK ON IT.

PAT.

DR. LEVITT: THANKS. JUST I THINK THREE THINGS. ONE IS PROGRAMMATIC CHANGES, MODIFICATIONS, WHICH SOUND LIKE THERE'S A LOT OF ENTHUSIASM FOR THINKING THIS THROUGH, REALLY NEEDS TO BE LINKED TO CHANGES IN HOW REVIEWS ARE DONE. THAT'S REALLY IMPORTANT. AND THE CASE STUDY IS THE R21 MECHANISM AT NIH, WHICH WAS ORIGINALLY DEVELOPED TO DO EXACTLY WHAT KEITH WAS TALKING ABOUT WITH HIS INTERNAL FUNDS, NO PILOT DATA NEEDED, GREAT IDEAS, ETC., AND IT MORPHED INTO THE SAME OLD, SAME OLD WITH -- AND IT'S JUST BEEN PERVERTED FROM MY PERSPECTIVE. AND I'VE BEEN ON MANY STUDY SECTIONS, A LOT OF YOU HAVE AS WELL. YOU SIT THERE AND SAY, WELL, BUT THE INSTRUCTIONS DON'T SAY YOU NEED PILOT DATA. AND THAT'S A CASE WHERE THERE'S A MISALIGNMENT BETWEEN WHAT THE PROGRAM WANTS TO SEE AND WHAT THE REVIEWERS ARE USED TO DOING. SO THAT'S A REALLY IMPORTANT THING, I THINK.

THE OTHER IS THAT ACADEMIC INSTITUTIONAL DOLLARS FOR WHAT WE USED TO DO IN TERMS OF INTERNAL SUPPORT TO GENERATE NEW IDEAS IS SHRINKING PRETTY

DRAMATICALLY, PARTICULARLY AT MEDICAL CENTERS WHERE HOSPITALS ARE STRUGGLING, ALL HOSPITALS. SO THAT'S SOMETHING TO KEEP IN MIND IN TERMS OF -- AS WE THINK ABOUT THE KINDS OF THINGS WE WOULD WANT TO IMPLEMENT.

AND THEN THE THIRD THING IS A METAPHOR FOR SPENDING MONEY THAT DOESN'T GET ONE ANYWHERE IS A WASTE OF MONEY, SO WE MIGHT AS WELL NOT SPEND IT. SO THE EXAMPLE I GIVE -- I DO A LOT OF POLICY TALKS ABOUT CHILD DEVELOPMENT, BRAIN DEVELOPMENT TO POLICYMAKERS, LEGISLATORS AND EDUCATORS, ETC. I SAID THE BIGGEST WASTE -- ONE OF THE BIGGEST WASTES OF MONEY IS THIS COUNTRY IS THE TEACHING OF FOREIGN LANGUAGE. WHY? BECAUSE IN ALMOST SCHOOL SYSTEMS, NOT ALL, BUT IN ALMOST ALL SCHOOL SYSTEMS, FOREIGN LANGUAGE IS INTRODUCED DURING PUBERTY, WHICH IS WELL PAST THE OPTIMAL TIME FOR THE BRAIN TO DEVELOP A SECOND LANGUAGE. AND IT'S BILLIONS OF DOLLARS THAT ARE SPENT ON TEACHING SECOND LANGUAGES AND THIRD LANGUAGES AT A TIME WHEN THE BRAIN IS COMPLETELY SUBOPTIMAL FOR LEARNING.

THERE'S AN EXAMPLE WHERE THEY SPEND A LOT OF MONEY. THE INTENTIONS ARE -- I UNDERSTAND THE INTENTIONS. SECOND LANGUAGES ARE REALLY IMPORTANT. SOMETIMES PEOPLE MISUNDERSTAND WHAT I'M SAYING.

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LEARNING A SECOND OR THIRD LANGUAGE IS GREAT. IT IMPROVES ONE'S MATHEMATICAL SKILLS AND COMPUTATIONAL AND COGNITIVE SKILLS. BUT LOOK AT WHERE IT'S BEING SPENT. SO WHATEVER WE DECIDE IN TERMS OF RECOMMENDATIONS TO THE BOARD WE HAVE TO THINK REALLY CAREFULLY ABOUT WHETHER WHAT WE'RE GOING TO SPEND IS REALLY OPTIMAL IN TERMS OF OUTCOME. IF IT'S INNOVATION AND A RECOGNITION THAT SOME OF THIS WILL FAIL, THAT'S OKAY AS LONG AS WE HAVE AN UNDERSTANDING OF HOW -- WHAT OUR GOALS ARE. THAT'S IT.

CHAIRMAN GOLDSTEIN: THANK YOU. MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: MARIA MILLAN BROUGHT UP A POINT ABOUT RARE DISEASE AND HOW THERE HAS BEEN SOME THINKING INTERNALLY ABOUT WHAT TO DO IN THAT AREA. SO, AGAIN, THIS IS AN INSTANCE WHERE UNDERSTANDING THE DIFFERENT THINGS THAT ARE BEING CONTEMPLATED INTERNALLY IS REALLY IMPORTANT BEFORE WE START A SUBJECT ABOUT PRIORITIZATION ONLY BECAUSE IF THERE ARE THINGS THAT THE TEAM BELIEVES ARE OR THEY'RE IN THE WORKS OR THEY'RE MOVING FORWARD OR THERE ARE CONSTANT PLANS THAT ARE BEING CONSIDERED, IT'S IMPORTANT FOR THE BOARD TO KNOW WHAT THOSE ARE. SO, MARIA, IN WHATEVER FORM WE CAN DO THAT, IT WOULD

BE HELPFUL, ESPECIALLY IF WHAT WE ARE STARTING TO DO IS GO DOWN A CONVERSATION ABOUT PRIORITIZATION BECAUSE RARE DISEASE IS CLEARLY IMPORTANT. WE'RE GOING TO DO A WORKSHOP. THE BOARD KNOWING ABOUT IT NOW IS GREAT. WE ARE STARTING DOWN A PATH OF STARTING TO TALK ABOUT THIS. SO IF THERE'S ANYTHING ELSE, IT'S IMPORTANT FOR THE BOARD TO UNDERSTAND WHAT THAT IS.

SO AN OVERVIEW OF WHAT'S PLANNED FOR THE NEXT YEAR OR SO WOULD PROBABLY A GOOD PLACE TO START AND AT LEAST HAVE A CONVERSATION WITH THE SCIENCE SUBCOMMITTEE.

CHAIRMAN GOLDSTEIN: GREAT POINTS, MARIA. THANK YOU.

OTHER COMMENTS? YOU KNOW I'D LIKE TO CIRCLE BACK TO MARK FISCHER-COLBRIE. SORRY FOR PUTTING YOU ON THE SPOT, MARK. WHAT DO YOU THINK WOULD BE APPROPRIATE NEXT STEPS FOR THIS COMMITTEE TO TAKE TO TRY TO ADDRESS SUBSTANTIVELY SOME OF THE ISSUES YOU BROUGHT UP? OR WHAT SORTS OF FURTHER CONVERSATIONS DO YOU THINK WE SHOULD HAVE?

DR. FISCHER-COLBRIE: I THINK WE NEED TO TAKE THIS INPUT AND CREATE A BIT OF A MATRIX WITH THE FEEDBACK AND PUT THAT DOWN ON PAPER AND USE THAT FOR THE NEXT JUMPING OFF POINT RELATED FOR HOW DO

YOU TRANSLATE THIS, IF AT ALL, BECAUSE YOU MIGHT DECIDE TO STAY THE COURSE, INTO ANY CHANGES RELATED TO THE CIRM PROCESS AND CIRM MECHANISM.

I THINK WHAT'S KIND OF EXCITING, THERE'S OBVIOUSLY BROAD SCALE POTENTIAL OPPORTUNITIES HERE. AND HAVING THAT NEXT FORMAL CONVERSATION ALONE WILL CONTINUE TO FEED IMAGINATION AND HAVE THE QUESTION OF WHAT'S THE RIGHT PROCESS, IF YOU WILL, FOR MAKING, IMPLEMENTING ANY CHANGES HERE BECAUSE THIS ISN'T NECESSARILY A SUBCOMMITTEE DRIVEN EVENT. THOSE ARE IDEAS AND INPUTS THAT WOULD BE FED INTO STAFF AND HAVE A MUTUAL FEEDBACK PROCESS LEADING TO BOARD CONCURRENCE AROUND THOSE ELEMENTS.

SO I THINK, LARRY, WOULD LIKE TO GET YOUR THOUGHTS AND YOUR FEEDBACK ON THIS. YOU KIND OF IN A WAY PIONEERED SOME OF THIS BY GOING THROUGH THE NEURO TASK FORCE ELEMENT. I WOULD LIKE TO GET YOUR SENSE AND OTHER'S SENSE ON, OKAY, THIS IS A GREAT CONVERSATION, A LOT OF FUN. HOW DO WE TRANSLATE THIS INTO ACTUALLY SOMETHING CONCRETE?

CHAIRMAN GOLDSTEIN: YES. GREAT POINT. IT'S EXACTLY WHAT WE NEED TO DO. QUESTION IS HOW TO GET THERE.

MARIA MILLAN, YOUR STAFF HAVE BEEN OBVIOUSLY THINKING VERY HARD ABOUT THESE SORTS OF

PROBLEMS. WOULD YOU BE WILLING TO HAVE A STAFF PRESENTATION TO THIS SUBCOMMITTEE, SAY, FOR AN OCTOBER OR NOVEMBER MEETING JUST TO KIND OF KEEP SOME MOMENTUM AND GET IT BUILDING?

DR. MILLAN: YES, ABSOLUTELY. FOR THE OCTOBER SCIENCE SUBCOMMITTEE MEETING, BRING IN SOME POTENTIAL AREAS FOR CONSIDERATION? I THINK THAT'S A GREAT IDEA BECAUSE I THINK IT ALSO, BY BRINGING IN SPECIFIC USE CASES, IT ALSO ADDRESSES SOME BROAD QUESTIONS THAT WERE BROUGHT UP IN THE OPENING PRESENTATION TODAY. SO --

CHAIRMAN GOLDSTEIN: GREAT. IT'S A DATE.

DR. MILLAN: IT'S A DATE. I CAN WORK WITH WHOEVER, MARK AND THE BOARD GOVERNANCE TEAM AND THEN MY TEAM TO KIND OF PROPOSE WHAT THAT WOULD LOOK LIKE AND THEN GET THAT ON THE AGENDA FOR OCTOBER.

CHAIRMAN GOLDSTEIN: GREAT. THAT WOULD BE GREAT BECAUSE I THINK THAT WILL HELP US KEEP SOME MOMENTUM AS WELL.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: IS THAT JUST FOR BIG IDEA AREAS, OR ARE WE GOING TO ALSO TALK ABOUT FUNDING LEVELS, THE PROPORTION OF DOLLARS THAT GO OUT TO THIS DIFFERENT PILLARS, THINGS LIKE THAT BECAUSE I THINK THAT'S ALSO PART OF WHAT WE NEED TO

LOOK AT TO UNDERSTAND SORT OF WHERE THE MONEY -- HOW THE MONEY GOES OUT, TO WHAT IT GOES OUT, AND HOW THAT CHANGES BASED ON ANY NEW IDEAS THAT COME IN. SO I THINK IT'S SORT OF IMPORTANT LOOK AT IN A BIG CONTEXT.

CHAIRMAN GOLDSTEIN: MY VIEW IS THAT WE OUGHT TO BE AGNOSTIC ABOUT THIS MOVING FORWARD AND LOOK FOR THE THINGS THAT WE THINK WILL HAVE THE HIGHEST IMPACT INDEPENDENT OF WHAT THE MECHANISM IS OR WHAT THE RIGHT TWEET IS. CIRM IS FUNDING A LOT OF REALLY GOOD STUFF, AND SOME OF IT HAS, IN FACT, MOVED THROUGH CLINICAL TRIALS AND INTO APPROVALS IN A FEW CASES. AND WE OBVIOUSLY WANT TO SEE MORE OF THAT. SO ANY ATTEMPT OR ANY APPROACH THAT WILL HELP US GET THERE I THINK WE OUGHT TO GET ON THE AGENDA AND TALK ABOUT. AND MARIA'S STAFF HAVE DONE A GREAT JOB OF IDENTIFYING IMPORTANT THINGS TO TALK ABOUT, AND THIS IS ONE OF THE MOST IMPORTANT TOPICS WE CAN DEAL WITH. I'M COMPLETELY AGNOSTIC ON HOW WE SHOULD TACKLE THIS.

OTHER THOUGHTS, COMMENTS? WE HAVE PLENTY OF AIRTIME AVAILABLE IF WE NEED IT. ALL RIGHT. SO CONVERSATION TO BE CONTINUED IN OCTOBER. PUBLIC MEETING, IT SOUNDS LIKE, ALSO COMING UP IN NOVEMBER. MARK, THANK YOU FOR THE EFFORT YOU'VE PUT INTO THIS.

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I THINK YOU'VE GOT THE DIALOGUE UP AND RUNNING, AND LET'S KEEP MOMENTUM BUILDING. I THINK WITH THAT, THANK YOU ALL FOR YOUR WORK TODAY. CIAO.

DR. FISCHER-COLBRIE: THANK YOU ALL. APPRECIATE IT.

(THE MEETING WAS THEN CONCLUDED AT 12:36 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 VIRTUAL PROCEEDINGS BEFORE THE SCIENCE SUBCOMMITTEE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON SEPTEMBER 1, 2023, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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