BEFORE THE
JOINT SCIENCE SUBCOMMITTEE AND
TASK FORCE ON NEUROSCIENCE AND MEDICINE
TO THE
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: MARCH 5, 2025
1 P.M.

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

FILE NO.: 2025-5

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I N D E X

ITEM DESCRIPTION	PAGE NO.
OPEN SESSION	
1. CALL TO ORDER	3
2. ROLL CALL	3
CLOSED SESSION	NONE
3. DISCUSSION OF CONFIDENTIAL INTELLECTUAL PROPERTY OR WORK PRODUCT, PREPUBLICATION DATA, FINANCIAL INFORMATION, CONFIDENTIAL SCIENTIFIC RESEARCH OR DATA, AND OTHER PROPRIETARY INFORMATION RELATING TO THE CLINICAL, TRANSLATIONAL, AND DISCOVERY PORTFOLIO. (HEALTH & SAFETY CODE 125290.30(F) (3) (B) AND (C)).	
OPEN SESSION	
4. UPDATE ON THE STRATEGIC ALLOCATION FRAMEWORK IMPLEMENTATION: NEW AND AMENDED	6
5. CONSIDERATION OF THE DISC5 PROGRAM CONCEPT	16
6. CONSIDERATION OF THE DISC4 PROGRAM CONCEPT	34
7. CONSIDERATION OF THE PRECLINICAL DEVELOPMENT PROGRAM CONCEPT	61
8. CONSIDERATION OF THE CLIN2 PROGRAM CONCEPT	86
9. PUBLIC COMMENT	NONE
10. ADJOURNMENT	104

MARCH 5, 2025; 1 P.M.

CHAIRMAN FISCHER-COLBRIE: SO WE CONTINUE TO MAKE SUBSTANTIAL PROGRESS TOWARDS THE STRATEGIC ALLOCATION FRAMEWORK AND A NUMBER OF OTHER ISSUES THAT WE'RE DEALING WITH TODAY. SO, SCOTT, IF YOU COULD CALL THE ROLL, THAT BE WOULD BE GREAT.

MR. TOCHER: THANK YOU VERY MUCH, MARK.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MR. TOCHER: LEONDRA CLARK-HARVEY. DEBORAH DEAS. MARK FISCHER-COLBRIE.

CHAIRMAN FISCHER-COLBRIE: HERE.

MR. TOCHER: ELENA FLOWERS.

DR. FLOWERS: PRESENT.

MR. TOCHER: JUDY GASSON.

DR. GASSON HERE.

MR. TOCHER: JEFF GOLDEN.

DR. GOLDEN: PRESENT.

MR. TOCHER: DAVID HIGGINS.

DR. HIGGINS: HERE.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: HERE.

MR. TOCHER: PAT LEVITT. SORRY, PAT. I THINK YOU'RE MUTED. PAT. WE'LL COME BACK. I CAN

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SEE THAT THE MIC IS MUTED STILL ON PAT.

CAROLYN MELTZER.

DR. MELTZER: PRESENT.

MR. TOCHER: PAT, I THINK YOU'RE THERE. IS YOUR MIC READY? CAN YOU HEAR ME?

CAROLYN MELTZER. DID I CALL YOU CAROLYN?

DR. MELTZER: YOU DID. PRESENT.

MR. TOCHER: THANKS. CHRIS MIASKOWSKI.

DR. MIASKOWSKI: PRESENT.

MR. TOCHER: MARV SOUTHARD.

DR. SOUTHARD: HERE.

MR. TOCHER: KAROL WATSON.

DR. WATSON: HERE.

MR. TOCHER: KEITH YAMAMOTO.

DR. YAMAMOTO: HERE.

MR. TOCHER: AND THE RECORD WILL REFLECT THAT PAT LEVITT IS ATTENDING THE MEETING. GREAT. THANKS. WE HAVE A QUORUM, MARK. READY TO PROCEED?

CHAIRMAN FISCHER-COLBRIE: GREAT. JUST AN IMPORTANT DATA POINT IN THE CONSIDERATION FOR WHAT IS HAPPENING HERE WITH THE OVERALL PROCESS, AND THAT'S WITHIN THE CONTEXT OF AN EXTRAORDINARY AMOUNT OF WORK AND COLLECTIVE TIME THAT HAS BEEN SPENT WITH A PROCESS TO WORK ON THE STRATEGIC ALLOCATION FRAMEWORK AND INHERENTLY THE PRIORITIZATIONS FOR

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CIRM AS A VEHICLE FOR DRIVING LEVERAGE AND WORKING EVEN MORE SUCCESSFULLY TOWARDS OUR COLLECTIVE GOALS AS STATED IN THE MISSION STATEMENT FOR CIRM.

AND WITHIN THAT CONTEXT, NOT ONLY HAS THE WORK BEEN A HERCULEAN EFFORT, IT'S ALSO A QUALITY THAT I THINK COULD BE REPRESENTED IN ACADEMIC JOURNALS IN THE CONTEXT THAT THESE ARE DECISIONS AND ALLOCATION ELEMENTS THAT MANY, MANY ORGANIZATIONS HAVE FACED, WHETHER IT'S PRIVATE OR PUBLIC INSTITUTIONS --

DR. LEVITT: HELLO. CAN YOU HEAR ME NOW?

CHAIRMAN FISCHER-COLBRIE: -- AND THE WORK HAS BEEN PHENOMENAL.

DR. LEVITT: I CAN'T HEAR YOU.

CHAIRMAN FISCHER-COLBRIE: OKAY. WE CAN HEAR YOU, PAT.

DR. LEVITT: HOW ABOUT NOW?

DR. YAMAMOTO: YEP.

DR. LEVITT: NOW I CAN HEAR YOU.

CHAIRMAN FISCHER-COLBRIE: OKAY. GREAT.

WITH THAT PREAMBLE TO REFLECT THE INCREDIBLE QUALITY OF THE WORK IS ALSO THE NEXT STEPS IN THE CONTEXT OF THE FINANCE SUBCOMMITTEE AND NEURO TASK FORCE REVIEW OF WHERE WE STAND AS THE NEXT STEP IN PROGRESSION TOWARDS DISCUSSION AND

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RECOMMENDATIONS TO THE BOARD WHICH IS UPCOMING HERE IN MARCH. SO IT'S A VERY IMPORTANT MEETING FOR THE SHAPING AND DETERMINATION FOR THAT ELEMENT. AND I APPRECIATE EVERYBODY'S TIME AND EFFORT IN DOING THAT. AND I LOOK FORWARD TO A WIDE-OPEN, FREE-RANGING DISCUSSION TO ENSURE THAT WE DO THE BEST JOB WE POSSIBLY CAN IN SHAPING THOSE COMMUNICATIONS TO THE BOARD IF REQUIRED.

SO WITH THAT, I'D LIKE TO TURN IT OVER TO J.T. FOR COMMENTS BEFORE WE GET INTO THE MEETING HERE.

MR. TOCHER: AND, MARK, JUST FOR THE RECORD REFLECT THAT DEBORAH DEAS AND LEONDRA CLARK-HARVEY ARE ATTENDING.

CHAIRMAN FISCHER-COLBRIE: GREAT. THANK YOU, SCOTT.

DR. THOMAS: THANK YOU, MARK, MEMBERS OF THE SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE, MEMBERS OF THE PUBLIC. IN OUR SEPTEMBER MEETING WHEN THE BOARD APPROVED THE STRATEGIC ALLOCATION FRAMEWORK, WHICH IS THE DOCUMENT THAT SET THE STAGE FOR DETERMINING HOW WE WERE GOING TO DEPLOY THE BALANCE OF OUR PROP 14 FUNDING, WE PROCEEDED TO PUT TOGETHER AN EFFORT THAT HAS LITERALLY INVOLVED VIRTUALLY EVERYBODY AT CIRM TO DEVELOP CONCEPT PLANS

FOR FOUR OF THE 13 CONCEPTS THAT WERE ADOPTED AT THE SEPTEMBER BOARD MEETING. AND THOSE ARE THE CONCEPTS WHICH YOU'RE GOING TO BE HEARING ABOUT TODAY FROM A NUMBER OF MEMBERS OF THE TEAM.

MY MESSAGE TO YOU IS JUST SIMPLY THAT THIS HAS BEEN AN EFFORT THAT WAS EXTREMELY SUBSTANTIAL, AS MARK HAS MENTIONED. THIS IS SOMETHING THAT IS, IN ADDITION TO MANY OTHER RESPONSIBILITIES THAT THE MEMBERS OF THE TEAM ALREADY HAD GOING FORWARD, WHICH MAKES THE WORK PRODUCT, IN MY OPINION, EVEN THAT MUCH MORE IMPRESSIVE. AND I THINK THAT OVER THE COURSE OF THIS DISCUSSION YOU WILL SEE THAT THERE HAS BEEN EXHAUSTIVE THOUGHT AS TO HOW TO BEST IMPLEMENT THE FOUR CONCEPTS THAT ARE GOING TO BE DISCUSSED, AND WE'LL FEEL THAT AT THE END OF THIS DISCUSSION THAT WE HAVE, I WOULD HOPE AND BELIEVE, A ROADMAP TO PROCEED WITH IMPLEMENTING WHAT WILL BE BROUGHT, NOT JUST TO TODAY, BUT TO MARCH'S BOARD MEETING.

I WANT TO CONGRATULATE THE MEMBERS OF ALL OF THE TEAMS, ALL THE PROGRAM GROUPS, PEOPLE YOU WILL BE HEARING FROM TODAY, AND ALL OF THE TEAM HERE AT CIRM, INCLUDING MEMBERS OF THE BOARD AS YOU HAVE STUCK WITH THIS THROUGH MANY, MANY MONTHS. THANK YOU FOR THAT. AND WITH THAT, I WANT TO TURN IT OVER

TO ROSA, WHO HAS OVERSEEN THIS ENORMOUS UNDERTAKING. AND I WANT, ROSA, TO PERSONALLY CONGRATULATE YOU AS WELL. SO PLEASE TAKE IT FROM HERE.

DR. CANET-AVILES: THANK YOU, J.T.

SO ALL THIS INTRODUCTION, I WANT TO ALSO THANK EVERYBODY FOR SPENDING THE TIME WITH US TO GO THROUGH WHAT WE HAVE PREPARED FOR YOU THIS AFTERNOON. AND I WANT TO PERSONALLY ACKNOWLEDGE THE INCREDIBLE EFFORT THAT HAS GONE INTO GETTING US TO THIS POINT. THIS HAS BEEN A REAL TEAM EFFORT. AND I WANT TO RECOGNIZE, NOT ONLY TODAY'S PRESENTERS AND LEADS OF THE DIFFERENT PARTS OF THE EFFORTS, BUT ALSO THE TEAMS FROM REVIEW AND COLLEAGUES FROM THE PROGRAMS TEAMS, THE TEAMS FROM GRANTS MANAGEMENT, LEGAL, AND BOARD GOVERNANCE AS WELL EVERYONE WHO HAS PLAYED A KEY ROLE IN SHAPING THESE CONCEPTS. AND I THINK IT'S IMPORTANT TO JUST TAKE A MINUTE TO ACKNOWLEDGE THIS.

A SPECIAL THANKS ALSO TO OUR SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE CO-CHAIRS. THANK YOU, MARK, CAROLYN, AND PAT. AND YOUR LEADERSHIP AND COMMITMENT AND TIME TO KEEPING WITH THE INVESTMENT STRATEGIES ARE IMPACTFUL ARE TRULY APPRECIATED. AND GOING THROUGH ALL THESE DIFFERENT PRECALLS HAS BEEN VERY HELPFUL IN SHAPING WHAT WE

ARE BRINGING TODAY.

I THINK I WANT TO TAKE A MINUTE TO MENTION THAT WHAT WE HAVE ACCOMPLISHED IN THE LAST FOUR MONTHS IS PRETTY REMARKABLE. TYPICALLY, AS A REMINDER, WE ARE ALL FAMILIAR WITH THE PROCESS. IT TAKES ABOUT A YEAR WITH MULTIPLE DISCUSSIONS ALONG THE WAY TO DEVELOP AND BRING A CONCEPT TO THE BOARD. AND I'D LIKE TO REMIND THIS BOARD OF THE STRATEGIC ALLOCATION FRAMEWORK PROCESS WHICH UNFOLDED OVER A PERIOD OF TWO YEARS. WE'VE HAD TO WORK FAST AND EFFICIENTLY TO ALIGN THESE PROPOSALS WITH OUR STRATEGIC GOALS AND GET THEM READY FOR YOUR CONSIDERATION IN MARCH AT THE BOARD MEETING.

THIS PACE WAS NECESSARY. I THINK WE ARE ALREADY AWARE OF WHAT'S GOING ON, NOT ONLY IN CALIFORNIA, BUT MORE AT THE FEDERAL LEVEL. AND IT'S BEEN NECESSARY TO KEEP THE MOMENTUM AS WELL WITH WHAT WE HAVE STARTED AND ENSURE CONTINUITY OF FUNDING AND SUPPORT OUR RESEARCH AND CLINICAL COMMUNITIES.

AS LIZ, DR. NOBLIN, WILL PRESENT IN HER PRESENTATION, TODAY'S DISCUSSIONS ARE JUST ONE PART OF A LARGER TIMELINE. EVERYTHING WE ARE DOING NOW IS BUILT ON THE ASSUMPTION THAT THESE CONCEPTS WILL MOVE FORWARD IN MARCH. WE UNDERSTOOD THAT THERE CAN

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BE DELAYS, BUT WE ALSO WANT TO BRING UP THAT REWORKING THE CALENDAR OR SHIFTING PROGRAM TIMELINES WILL PUSH BACK FUTURE FUNDING OPPORTUNITIES SINCE EVERYTHING IS INTERCONNECTED. AND WE WANT TO BE MINDFUL OF THAT AS WE MOVE FORWARD.

NOW, WHAT ARE WE BRINGING TO TODAY'S MEETING? TODAY WE ARE ROLLING OUT THE FIRST IMPLEMENTATION OF CIRM'S STRUCTURED PREFERENCE-SETTING PROCESS, WHICH IS FRAMEWORK THAT HELPS KEEP FUNDING PRIORITIES DYNAMIC, DATA DRIVEN, AND ALIGNED WITH THE MATCHING OPPORTUNITIES AND PORTFOLIO NEEDS. AND THIS, VERY IMPORTANTLY, BUILDS ON THE NEURO TASK FORCE MODEL, WHICH WAS ORIGINALLY DEVELOPED TO GUIDE CIRM'S NEUROSCIENCE INVESTMENTS UNDER PROPOSITION 14.

NOW, WE ARE EXPANDING AND INCLUDING THAT STRUCTURED APPROACH ACROSS THE ENTIRE REGENERATIVE MEDICINE SPACE, INCLUDING PROP 14'S NEURO MANDATE AND BROADER CELL AND GENE THERAPY PRIORITIES.

FOR TODAY, WHICH IS THIS FIRST BOX THAT WE SEE HERE, WE ARE GOING TO BRING THE NEW CONCEPTS AND INTEGRATE FOCUS AREAS AND PREFERENCE SETTING INTO BRINGING THESE CONCEPTS. AND YOU WILL SEE IT IN THE PRESENTATION. WE'VE BEEN USING A DATA-DRIVEN APPROACH TO IDENTIFY PORTFOLIO GAPS, EMERGING

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SCIENCE, AND REGULATORY TRENDS THAT HAVE DRIVEN THIS PREFERENCE SETTING. AND WE ARE ALSO PRIORITIZING HIGH IMPACT RESEARCH AREAS AND UNMET CLINICAL NEEDS TO ENSURE THAT CIRM FUNDING AND STRATEGY IS AS STRATEGIC AND EFFECTIVE AS POSSIBLE.

NOW, IN JUNE WE ARE GOING TO BRING ANOTHER PRESENTATION. WHAT WE WILL COME WITH TO YOU IN JUNE IS THIS WILL EVOLVE INTO A FORMALIZED ANNUAL PORTFOLIO PROGRAM PERFORMANCE REVIEW TOWARDS THE END OF THE FISCAL YEAR. THIS YEAR WE ARE COMING SEPARATE. WE ARE COMING WITH THE CONCEPTS NOW, AND THEN THE PORTFOLIO IN JUNE. AND THE MAIN REASON WAS A TIME ISSUE HERE, BUT WE'VE IMPLEMENTED A LOT OF WHAT WE'VE BEEN ANALYZING INTO THE CONCEPTS. RIGHT.

NOW, WE WILL BE BRINGING COMPREHENSIVE ASSESSMENT OF CURRENT AWARDS, RESEARCH PROGRESS, AND FUNDING GAPS IN JUNE. AND THEN THE SCIENCE COMMITTEE AND THE ICOC EVERY YEAR, AT THE END OF THE FISCAL YEAR, WE'LL REVIEW PROPOSED ADJUSTMENTS TO FUNDING PRIORITIES WHICH WILL THEN BE INCORPORATED INTO NEXT YEAR'S FUNDING CYCLES. THE GOAL IS TO KEEP CIRM'S FUNDING APPROACH FLEXIBLE AND FORWARD LOOKING WHILE STAYING ALIGNED WITH THE SAF. THIS PREFERENCE-SETTING PROCESS AS OUTLINED IN THE EXHIBIT A OF THE MEMO FOR THE CONCEPTS IS A BIG STEP

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TOWARDS MAXIMIZING THE IMPACT OF CIRM'S INVESTMENTS AND ENSURING THAT REGENERATIVE MEDICINE FUNDING STAYS STRATEGIC, RESPONSIVE, AND POSITIONED FOR SUCCESS.

SO WE LOOK FORWARD TO THE DISCUSSION AND YOUR INSIGHTS TODAY. AND WITHOUT LESS FURTHER ADO, UNLESS THERE ARE ANY QUESTIONS ABOUT THIS, I WOULD LIKE TO LEAD ON TO DR. NOBLIN FOR HER SAF PRESENTATION.

DR. NOBLIN: THANK YOU ALL VERY MUCH. TODAY I WILL GIVE A VERY BRIEF BACKGROUND ON OUR CONCEPT DEVELOPMENT PROCESS AND THEN HAND IT OVER TO MY COLLEAGUES IN TURN TO TALK THROUGH THE DISC5, DISC4, PDEV, AND CLIN2 CONCEPTS.

SO BY MEANS OF INTRODUCTION, TODAY I'LL COVER HOW THE NEW CONCEPTS YOU'LL HEAR ABOUT RELATED TO CIRM'S IMPACT GOALS IN THE SAF, BRIEFLY TALK THROUGH THE CONCEPT DEVELOPMENT PROCESS, AND THEN SHOW THE LAUNCH TIMELINE THAT WE'VE BEEN REFERRING TO IN THIS INTRODUCTION.

IN SEPTEMBER OF LAST YEAR, THE ICOC APPROVED THE STRATEGIC ALLOCATION FRAMEWORK. AND THIS FRAMEWORK INCLUDED A SET OF GOALS TO MAXIMIZE CIRM'S IMPACT IN THE REGENERATIVE MEDICINE SPACE. THE GOALS WERE ORGANIZED INTO FOUR CATEGORIES; AND

IN ADDITION TO THE IMPACT GOALS THEMSELVES, THE SAF INCLUDED RECOMMENDATIONS FOR CONCEPT DEVELOPMENT TO ACHIEVE THOSE GOALS.

THE CONCEPTS THAT YOU WILL HEAR ABOUT TODAY ARE FOCUSED ON GOAL 1, WHICH IS TO CATALYZE THE IDENTIFICATION AND VALIDATION OF AT LEAST FOUR NOVEL TARGETS AND BIOMARKERS, ENSURING INTEGRATION INTO PRECLINICAL OR CLINICAL RESEARCH FOR DISEASES IN CALIFORNIA, AS WELL AS GOAL 4, WHICH IS TO PROPEL 15 TO 20 THERAPIES TARGETING DISEASES AFFECTING CALIFORNIANS TO LATE STAGE TRIALS. AND BY DESIGN, THE CONCEPTS THAT YOU WILL HEAR ABOUT TODAY INCORPORATE ELEMENTS OF GOAL 5, WHICH IS TO ENSURE THAT EVERY BLA-READY PROGRAM HAS A STRATEGY FOR ACCESS AND AFFORDABILITY.

FOLLOWING APPROVAL OF THE SAF AT THE ICOC MEETING IN SEPTEMBER OF LAST YEAR, WE'VE BEEN FULLY FOCUSED ON DEVELOPING THE CONCEPTS THAT ARE IN THIS INITIAL PHASE. AND ASSUMING ICOC APPROVAL AT THE END OF MARCH, WE'RE ALSO POISED TO OPEN ALL OF THESE FUNDING OPPORTUNITIES AS SOON AS POSSIBLE FOR THE REMAINDER OF THIS CALENDAR YEAR. AND IN ADDITION TO OPENING THESE FUNDING OPPORTUNITIES, WE WOULD THEN TURN OUR ATTENTION TO THE DEVELOPMENT OF THE NEXT PHASE OF CONCEPTS. AND THIS IS ALL CONCURRENT WITH

CONTINUING TO MANAGE AND EVALUATE THE FUNDING OPPORTUNITIES THAT REMAIN OPEN AND OUR ACTIVE AWARD PORTFOLIO.

THIS SCHEMATIC WALKS THROUGH OUR PROCESS FOR DEVELOPING THE CONCEPTS THAT YOU WILL HEAR ABOUT TODAY. WE STARTED WITH THE IMPACT GOALS AND RECOMMENDATIONS THAT EMERGED FROM THE SAF. AND WE FOLLOWED A DATA-DRIVEN APPROACH INCORPORATING BOTH THE RECOMMENDATIONS FROM THE SAF AS WELL AS ANALYSIS OF CIRM'S PORTFOLIO AND THE REGENERATIVE MEDICINE LANDSCAPE TO ARRIVE AT THE CONCEPT DESIGNS THAT YOU WILL HEAR ABOUT TODAY. AND THIS PORTFOLIO ANALYSIS AND LANDSCAPE ANALYSIS ARE WHAT INFORMS THE PREFERENCES THAT ARE INCORPORATED INTO THREE OUT OF THE FOUR CONCEPTS WHICH WE WILL GO THROUGH.

NOW, FOR A VERY BRIEF SNAPSHOT, THE FOUR CONCEPTS YOU WILL HEAR ABOUT TODAY COVER CIRM'S DISCOVERY, PRECLINICAL DEVELOPMENT, AS WELL AS CLINICAL DEVELOPMENT STAGES IN THE R&D PROCESS.

ON THE DISCOVERY SIDE, THE TWO COMPLEMENTARY PROGRAMS, DISC5 AND DISC4, BOTH EMPHASIZE TEAM SCIENCE TO ARRIVE AT NOVEL DISCOVERIES IN REGENERATIVE MEDICINE WITH DISC4 HAVING AN EMPHASIS ON LARGE TEAMS FOLLOWING THE REMIND MODEL AND DISC5 ENABLING SMALLER TEAMS.

PDEV IS A NEW CONCEPT, WHICH IS A CONSOLIDATION OF PRIOR FUNDING OPPORTUNITIES ADDRESSING THE PRECLINICAL SPACE AND AIMS TO ADVANCE PROMISING CANDIDATES THROUGH IND. AND IN PDEV YOU'LL HEAR ABOUT CANDIDATE PREFERENCES THAT ARE ALIGNED TO SAF GOALS. AND ON THE CLINICAL SIDE, WE'LL HAVE AN UPDATE TO OUR CLIN2 FUNDING OPPORTUNITY, AND THOSE UPDATES REFLECT INCORPORATING THE SAF RECOMMENDATIONS AS WELL AS PREFERENCE SETTING.

AND THEN TO CLOSE THIS INTRODUCTION, THIS SLIDE HERE IS OUR SNAPSHOT OF WHAT THE YEAR AHEAD LOOKS LIKE FOR US ASSUMING ICOC APPROVAL OF THESE FOUR NEW CONCEPTS AT THE END OF MARCH. WE HAVE WORKED WITH OUR COLLEAGUES AND ARE POISED TO OPEN FUNDING OPPORTUNITIES IN DISCOVERY, PDEV, AND CLIN2 IN THE SPRING PENDING ICOC APPROVAL.

MR. TOCHER: LIZ, I'M SORRY. LEONDRA CLARK-HARVEY HAS HER HAND RAISED.

DR. NOBLIN: OH, OF COURSE. GO AHEAD.

DR. CLARK-HARVEY: SORRY TO INTERRUPT. I JUST WANT TO MAKE SURE THAT I CAUGHT THE NAME CORRECTLY. SO THE NEW PDEV, DOES THAT STAND FOR PRECLINICAL DEVELOPMENT? DID I GET IT RIGHT?

DR. NOBLIN: YES.

DR. CLARK-HARVEY: OKAY. PERFECT. THANK YOU. I APPRECIATE THAT.

DR. NOBLIN: SO FOLLOWING THE OPENING OF APPLICATIONS IN THE SPRING, WE'RE THEN SET TO BEGIN GRANTS WORKING GROUP REVIEWS OF THE NEW CONCEPTS IN THE FALL. AND THIS IS CONCURRENT WITH THE CONTINUATION OF THE DISC-0 FUNDING OPPORTUNITY, WHICH IS ACTIVE, AND THE CCCE CONCEPT, WHICH IS IN DEVELOPMENT AND WILL BE GOING THROUGH THE AAWG FOR BOARD APPROVAL IN MARCH.

SO UNLESS THERE ARE FURTHER QUESTIONS, I WILL HAND IT OVER TO DR. SHEPARD FOR AN OVERVIEW OF THE DISC5 CONCEPT.

DR. SHEPARD: GOOD AFTERNOON, EVERYONE, MEMBERS OF THE SCIENCE SUBCOMMITTEE, NEURO TASK FORCE, MEMBERS OF THE PUBLIC, AND THE CIRM TEAM. IT'S MY PLEASURE TO KICK OFF THE SERIES OF DISCUSSIONS ON THESE CONCEPTS THAT WE ARE BRINGING FOR YOUR CONVERSATION TODAY.

I'D LIKE TO BEGIN BY JUST GOING -- GIVING A BRIEF OVERVIEW OF THE CONTENTS OF MY PRESENTATION BECAUSE THIS WILL BE A FORMAT THAT WE ALL FOLLOW TODAY. SO WE'LL START WITH A GENERAL BACKGROUND AND INTRODUCTION AND EXPLAIN HOW THIS NEW PROGRAM ALIGNS WITH THE IMPACT GOALS THAT LIZ JUST

DESCRIBED. WE'LL BRIEFLY GO OVER THE OBJECTIVE OF THIS PROGRAM AS WELL AS THE SCOPE AND STRUCTURE, WHICH INCLUDES INFORMATION ABOUT THE AWARD BUDGET, THE PROJECT ELIGIBILITY, AND TEAM ELIGIBILITY, AS WELL AS OTHER TYPES OF CHANGES AND IMPROVEMENTS THAT WE ARE DEVELOPING AND PROPOSING. AND FINALLY, WE WILL FOLLOW WITH A REQUEST FOR YOUR RECOMMENDATION TO THE FULL BOARD MEETING AT THE END OF MARCH.

OKAY. SO JUST -- I WON'T GO IN TOO MUCH DETAIL OVER THIS BECAUSE ROSA AND LIZ NICELY WENT OVER THIS, BUT I JUST WANT TO REMIND YOU THAT THE IMPACT GOAL THAT THIS PROGRAM IS DESIGNED TO ADDRESS IS TO CATALYZE THE IDENTIFICATION AND VALIDATION OF AT LEAST FOUR TARGETS, NOVEL TARGETS AND BIOMARKERS, AND ENSURING INTEGRATION INTO PRECLINICAL OR CLINICAL RESEARCH PROGRAMS. AND THE RECOMMENDATION TO ACHIEVE THIS GOAL WAS TO SUPPORT COMPREHENSIVE DISCOVERY THROUGH DISC4 AND DISC5 FUNDING STRUCTURES.

SO THE OBJECTIVE, THEN, OF BOTH OF THESE PROGRAMS, DISC5 AND DISC4, WHICH YOU WILL HEAR ABOUT NEXT, APPLY A COMMON OBJECTIVE, WHICH IS TO SUPPORT COMPREHENSIVE DISCOVERY RESEARCH ACROSS A DIVERSE RANGE OF DISEASES AND BOTTLENECKS TO ACCELERATE THE DEVELOPMENT OF POTENTIAL THERAPEUTICS AND BIOMARKERS

IN REGENERATIVE MEDICINE. SO THESE TWO AWARD STRUCTURES THAT YOU WILL BE HEARING ABOUT PROVIDE COMPLEMENTARY APPROACHES TO MEETING THIS COMMON OBJECTIVE. AND THIS IS BRIEFLY ILLUSTRATED ON THE SLIDE HERE. DISC4 WILL BE DESCRIBING LARGE, MULTIDISCIPLINARY COLLABORATIONS, AND DISC5 IS FOCUSED ON SMALLER MULTIDISCIPLINARY, COLLABORATIVE APPROACHES.

MS. MANDAC: JEFF HAS HIS HAND RAISED. JEFF GOLDEN.

DR. SHEPARD: SORRY. DR. GOLDEN.

DR. GOLDEN: I JUST HAD A QUESTION. ON THIS SLIDE IN DISC4 YOU SAY TO FACILITATE TARGET AND BIOMARKER IDENTIFICATION, BUT IT SEEMS LIKE THAT WOULD BE EQUALLY LIKELY IN DISC5.

DR. SHEPARD: YES.

DR. GOLDEN: ARE YOU SUGGESTING THAT ONE IS TARGETED ON ONE OR THE OTHER, OR DO THEY CROSS OVER TO BOTH OF THOSE?

DR. SHEPARD: I'M SORRY IF I DIDN'T ELABORATE CLEARLY ENOUGH. BOTH OF THESE PROGRAMS ADDRESS THE SAME GOAL AND TO LEAD TO DISCOVERY OF TARGETS AND BIOMARKERS, BUT THEY'RE TAKING COMPLEMENTARY APPROACHES SO THAT THEY ARE WORKING TOGETHER AND INDIVIDUALLY TOWARDS IMPACTING THIS

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GOAL THROUGH ELUCIDATING DISEASE MECHANISMS AND OTHER RESEARCH THAT I'LL GO OVER IN MY SUBSEQUENT SLIDES. BUT WE WANTED TO INTRODUCE THIS SINCE THERE'S THIS COMMON OBJECTIVE BETWEEN THE TWO PROGRAMS THAT YOU'RE GOING TO BE HEARING ABOUT THAT ARE INTENDED TO WORK TOGETHER. AND IN ADDITION TO WORKING TOGETHER, THEY'RE DESIGNED TO WORK WITH INFRASTRUCTURE THAT'S BEEN DEVELOPED ACROSS A BROADER SET OF PROGRAMS, INCLUDING OUR ALPHA CLINICS AND OUR EDUCATIONAL PROGRAMS, AND EVEN SOME PROGRAM INFRASTRUCTURE THAT'S BEING PILOTED THROUGH THE REMIND AWARDS THAT WERE RECENTLY LAUNCHED.

AND THE IDEA BEHIND THIS IS THAT BY LEVERAGING INTERNAL/EXTERNAL PARTNERSHIPS AND OTHER CIRM-FUNDED RESOURCES, WE CAN MAXIMIZE OR EVEN INCREASE THE IMPACT OF THE OUTCOMES OF THESE AWARDS BEYOND WHAT THE RESEARCH ITSELF ENTAILS.

DR. GOLDEN: OKAY. SO JUST TO BE CLEAR, AN APPLICATION IN DISC5 COULD STILL INCLUDE THE DISCOVERY OF BIOMARKERS FOR TARGETS EQUAL TO WHAT DISC4 DOES; IS THAT CORRECT?

DR. SHEPARD: THE TYPES OF APPROACHES AND QUESTIONS ADDRESSED, YES, OR COULD BE EXACTLY THE SAME, BUT THE SCALE OF THE RESEARCH THAT THESE PROGRAMS WILL SUPPORT IS WHERE THE DIFFERENCE IS.

DR. GOLDEN: GREAT. THANK YOU.

DR. SHEPARD: SO NOW WE'LL GO A BIT MORE INTO THE SPECIFIC DETAILS OF WHAT SETS DISC5 APART FROM THE OTHER PROGRAMS. SO JUST TO REPEAT, THE OBJECTIVE IS TO SUPPORT COMPREHENSIVE DISCOVERY RESEARCH ACROSS DIVERSE RANGES OF DISEASES AND TECHNICAL BOTTLENECKS, ACCELERATE THE DEVELOPMENT OF POTENTIAL THERAPEUTICS AND BIOMARKERS IN REGENERATIVE MEDICINE. AND THE APPROACH WILL BE TO SUPPORT EXPLORATORY AND INNOVATIVE FOUNDATIONAL RESEARCH LED BY SMALL TEAMS OF INVESTIGATORS.

SO THE SCOPE OF THESE AWARDS IS COMPRISED IN THIS LIST OF EXPECTED OUTCOMES. SO ALL DISC5 AWARDS WILL SUPPORT EXPLORATORY AND INNOVATIVE FOUNDATIONAL RESEARCH, BUT THEY WILL BE LED BY PAIRS OF INVESTIGATORS. AND THE IDEA IS TO ACHIEVE ONE OR MORE OF THE FOLLOWING OUTCOMES: ADVANCING OUR UNDERSTANDING OF HUMAN STEM AND PROGENITOR CELLS AS THEY PERTAIN TO HUMAN HEALTH AND DISEASE. ADVANCING THE USE AND IMPACT OF STEM CELLS, AND THE EXPLORATION OF DISEASE MECHANISMS AND THERAPEUTIC TARGET DISCOVERY. IDENTIFYING BIOLOGICAL INSIGHTS TO ADDRESS KEY BOTTLENECKS IN STEM CELL AND GENE THERAPY AND OTHER REGENERATIVE MEDICINE APPROACHES. AND ADVANCING THE APPLICABILITY OF STEM CELL AND

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GENE THERAPY AND OTHER REGENERATIVE MEDICINE APPROACHES TO DIVERSE HUMAN POPULATIONS.

SO IF THIS SOUNDS A LITTLE BIT FAMILIAR TO YOU, IT'S NOT SURPRISING BECAUSE DISC5 IS BASICALLY A RESPONSE OF THE STRATEGIC ALLOCATION FRAMEWORK TO BUILD OFF THE SUCCESSFUL FOUNDATIONAL DISC-0 PROGRAM THAT WE'VE BEEN OPERATING FOR THE PAST COUPLE OF YEARS, BUT INCREASE ITS EFFECTIVENESS BY ALIGNING IT TO THE NEW GOALS. SO IT'S BASICALLY SIMPLIFYING, IMPROVING, AND BUILDING UPON THE DISC-0 STRUCTURE TO ENCOURAGE SMALL COLLABORATIONS AND ENHANCE THE SUPPORT FOR THE MORE EXPLORATORY SIDE OF THIS RESEARCH.

SO HOW IS IT DIFFERENT FROM DISC-0? WE'RE GOING TO GO INTO THAT IN A LITTLE BIT MORE DETAIL, BUT IT BOILS DOWN TO THE TWO FOLLOWING THINGS. ONE, THERE IS A MUCH GREATER EMPHASIS ON COLLABORATION. SO RATHER THAN BEING LED BY A SINGLE PRINCIPAL INVESTIGATOR, AS WAS THE CASE IN OUR FIRST TRACK OF DISC-0, DISC5 WILL SUPPORT A CORE TEAM COMPRISING A PAIR OF INVESTIGATORS WITH EQUAL LEADERSHIP TO THE TEAM. SO BASICALLY IT'S A JOINT LEADERSHIP, AND THEY'RE EXPECTED TO BRING DIFFERENT PERSPECTIVES OR DISCIPLINES TO A PROBLEM TO CREATE A NEW WAY OF LOOKING AT THINGS, NEW PERSPECTIVES TO OPEN NEW

DOORS INTO RESEARCH.

THE SECOND AREA IS WE'RE ENHANCING THE SUPPORT AND WEIGHT THAT INNOVATION TAKES SO THAT THAT EARLIER MORE STAGED EXPLORATORY PROGRAMS THAT MAY BE HIGH RISK, HIGH REWARDS CAN BE SUPPORTED THROUGH THIS PROGRAM.

OKAY. SO THIS SLIDE IS A BIT OF A PUNCH LINE BECAUSE THIS DESCRIBES EVERYTHING THAT I'M GOING TO GO OVER IN MY NEXT FEW SLIDES. BUT A COUPLE OF THINGS I WANTED TO JUST HIGHLIGHT BEFORE I GO INTO MORE DETAIL IS THAT THESE PROGRAMS WILL BE OFFERED ONCE A YEAR. THE GRANTS ARE DESIGNED TO PROVIDE SUPPORT FOR THREE YEARS IN DURATION. IT WILL BE OPEN TO CALIFORNIA NON-PROFIT OR FOR-PROFIT RESEARCH INSTITUTIONS. IT WILL BE LED BY A TEAM OF TWO PRINCIPAL INVESTIGATORS, WHICH BY DESIGNATION ARE CALLED THE PI, CO-PI FOR REASONS I'LL GO INTO. A MAXIMUM AWARD TOTAL OF $2.5 MILLION. AND WE ANTICIPATE THAT AN ALLOCATION OF $50 MILLION WOULD SUPPORT APPROXIMATELY 15 TO 20 OF THESE AWARDS.

SO THE FIRST THING I'D LIKE TO HIGHLIGHT IS THE TOTAL COST CAP. ONE DIFFERENCE BETWEEN THIS DISC5 PROGRAM AND DISC-0 IS THAT WE ARE OFFERING A TOTAL AWARD CAP RATHER THAN A DIRECT PROJECT COST CAP. WHILE THE OVERALL AWARD AMOUNT IS SIMILAR, BY

USING THE TOTAL COST CAP, IT REMOVES A DISINCENTIVE FOR MULTI-INSTITUTIONAL COLLABORATIONS. AND WE WANTED TO MAKE THAT CHANGE BECAUSE WE WANT TO REALLY ENCOURAGE MULTI-INSTITUTIONAL COLLABORATIONS THROUGH THIS PROGRAM.

IN TERMS OF PROJECT ELIGIBILITY, IN ORDER FOR SOMEONE TO APPLY, THEIR PROJECT MUST ADDRESS KEY KNOWLEDGE GAPS OR RESEARCH BOTTLENECK THAT COULD LEAD TO ONE OR MORE OF THE EXPECTED OUTCOMES THAT I HIGHLIGHTED EARLIER. IT SHOULD FOCUS ON STUDIES THAT EMPLOY HUMAN STEM CELLS AND/OR GENETIC RESEARCH AS PART OF THE CENTRAL APPROACH OR HYPOTHESIS. AND IF IT'S NECESSARY TO USE ANY NONHUMAN MODELS, PROVIDE A STRONG JUSTIFICATION FOR THAT.

IN TERMS OF TEAM ELIGIBILITY, AS I MENTIONED, IT'S OPEN TO ALL CALIFORNIA RESEARCH INSTITUTIONS WHETHER THEY BE NON-PROFIT OR FOR-PROFIT. THE CORE TEAM MUST COMPRISE TWO CALIFORNIA-BASED INVESTIGATORS THAT BOTH CONTRIBUTE AT LEAST 5-PERCENT EFFORT. THE DIFFERENCE IN DESIGNATION IS THAT THE PRINCIPAL INVESTIGATOR IS THE ONE WHO ACTS AS THE MAIN POINT OF CONTACT WITH CIRM STAFF FOR ADMINISTRATIVE PURPOSES. AT THE LEVEL OF SCIENTIFIC LEADERSHIP, BOTH OF THESE INVESTIGATORS ARE CONTRIBUTING EQUALLY TO THE

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PROJECT.

IN TERMS OF THE APPLICATION REVIEW PROCESS, DISC5 WILL UTILIZE THE ESTABLISHED TWO-STAGE REVIEW PROCESS THAT WE HAVE BEEN USING FOR SEVERAL YEARS NOW FOR OUR DISCOVERY STAGE PROGRAMS, WHICH ALLOWS US TO EFFECTIVELY MANAGE HIGH APPLICATION VOLUMES BECAUSE WITH THESE DISCOVERY PROGRAMS THAT WE'LL SEE HOPEFULLY. AND IN ADDITION SOME IMPROVEMENTS AND ENHANCEMENT TO OUR REVIEW PROCESS WILL ENHANCE WEIGHT AND VISIBILITY FOR INNOVATION. AS WE MENTIONED, WE WANT TO INCREASE THE LIKELIHOOD OF HIGH RISK, HIGH REWARD PROPOSALS RECEIVING MERITORIOUS FUNDING DECISIONS, AND IMPROVE GRANULARITY AND VISIBILITY FOR SCORE-DRIVING DECISIONS.

NOW, OTHER ATTRIBUTES AND IMPROVEMENTS INCLUDE MAINTAINING THE DATA SHARING AND MANAGEMENT PLAN REQUIREMENT THAT WAS INTRODUCED IN OUR DISCOVERY-0 OR FOUNDATIONAL AWARD PROGRAM AND CONTINUING TO ITERATE ON THE DATA SHARING AND MANAGEMENT IMPROVEMENTS AS CIRM DEVELOPS ITS DATA SHARING INFRASTRUCTURE. AND THAT, OF COURSE, INVOLVES REQUIRING THE COORDINATION WITH CIRM'S DATA INITIATIVES.

THIS IS JUST A SNAPSHOT OF THE TIMELINE

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THAT DR. NOBLIN PRESENTED EARLIER SHOWING THAT IF THIS CONCEPT IS APPROVED AT THE MARCH BOARD MEETING, WE WOULD MOVE ON TO POSTING THE PROGRAM ANNOUNCEMENT SHORTLY THEREAFTER AND OPENING THE COMPETITION SUCH THAT APPLICATIONS WOULD BE RECEIVED IN NOVEMBER. I KNOW NOVEMBER MIGHT SEEM LIKE A WAYS AWAY, BUT I ALSO WANT TO REMIND YOU THAT WE HAVE OUR DISC-0 FUNDING OPPORTUNITY THAT HAS APPLICATIONS DUE IN APRIL. SO WE DO HAVE OPPORTUNITIES THROUGHOUT THE YEAR FOR SMALL TEAMS AND SMALLER SCALE PROJECTS TO APPLY FOR SUPPORT OF THEIR NOVEL AND INNOVATIVE PROJECTS THROUGH OUR PROGRAMS.

AND WITH THAT, WE WOULD REQUEST A MOTION THAT THE SCIENCE COMMITTEE/NEURO TASK FORCE RECOMMEND APPROVAL TO THE FULL ICOC OF THIS DISC5 CONCEPT. BUT BEFORE THAT, I'D BE HAPPY TO TAKE ANY QUESTIONS THAT WOULD HELP YOUR DISCUSSION.

DR. SOUTHARD: THAT WE BE -- OH, THERE'S A QUESTION. PAT HAS A QUESTION.

DR. LEVITT: DO YOU WANT ME TO WAIT UNTIL THERE'S A MOTION AND THEN COMMENT? I'M FINE WITH THAT.

MR. TOCHER: NO, PAT. YOU CAN PROCEED WITH YOUR QUESTION, AND THEN JUDY WILL FOLLOW.

DR. LEVITT: SO I WENT THROUGH THE SLIDES

AGAIN, AND WE HAD THIS CONVERSATION. WE HAD THE PREMEETING. THIS IS LIKE ONE OF THE REMIND -- THIS IS THE SMALLER VERSION OF THE REMIND THAT'S BEEN QUITE SUCCESSFUL, WHICH IS THE INVESTMENTS IN NEURO-RELATED RESEARCH IN ACCORDANCE WITH PROPOSITION 14. THE SLIDES THAT I REVIEWED, NEURO IS BEING INTEGRATED WITHIN THIS AND THE OTHER APPROACHES THAT WE'RE GOING TO HEAR ABOUT.

I'M ALL IN FAVOR OF THE APPROACH. I'M STILL QUITE WORRIED ABOUT WE HAVE A PROPOSITION THAT HAS AN IDENTIFICATION OF A SPECIFIC DOMAIN OF INVESTMENT THAT'S QUITE SIZABLE. WE HAVE A TASK FORCE THAT WAS IMPLEMENTED TO DEAL WITH THAT SPECIFICALLY SEPARATE FROM THE SCIENCE SUBCOMMITTEE. BUT WE HAVE, FROM MY PERSPECTIVE, A MISALIGNMENT IN TERMS OF WHAT WE'RE GOING TO DO WITH THESE NEW FUNDING APPROACHES.

THE FUNDING APPROACHES ARE GREAT, BUT I THINK, FROM MY PERSPECTIVE, IT'S NOT ALIGNED WITH WHAT WE KNOW ARE THINGS THAT WE'RE GOING TO HAVE TO ACCOMPLISH WITHIN A RELATIVELY MODEST PERIOD OF TIME. SO I DON'T KNOW HOW TO ADDRESS THIS OTHER THAN TO SAY THAT I'M CONCERNED ABOUT THIS MISALIGNMENT.

DR. CANET-AVILES: THANK YOU, PAT. SO AS

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PART OF THE -- WE HAVEN'T YET GONE THROUGH THE DISC4 PRESENTATION. AND FOR THIS ONE WE ARE AN ALL ENCOMPASSING SCOPE OF THE APPLICATIONS, AND THIS IS A SMALLER AMOUNT OF MONEY. THEY ARE IN SCALE MUCH SMALLER AWARDS. I THINK THAT THE NEURO TASK FORCE DISCUSSION OF PREFERENCES COULD HAVE A SWING INTO THE DISC4. WE ARE GOING TO GO -- DR. LEK TAN IS GOING TO BE PRESENTING THIS. AND IN THAT CASE THERE ARE SOME AREAS, PREFERENCES THAT WE COULD SET UP THAT WOULD VERY MUCH ALIGN WITH THE NEURO TASK FORCE. AND I THINK THERE ARE DIFFERENT LEVELS OF OPPORTUNITIES OF WHERE WE CAN DO THAT.

ANOTHER COMMENT I WOULD LIKE TO MAKE IS THAT IN TERMS OF SPENDING, AND I KNOW THIS DOES NOT ANSWER EVERYTHING, BUT AT THE RATE WE ARE SPENDING ON NEURO PROJECTS, WE ARE RIGHT NOW OVER THE -- IF WE KEEP GOING AT THIS RATE, BY THE TIME CIRM COULD END ITS FUNDING, WE COULD HAVE OVERSPENT OVER $1.5 BILLION FOCUSED ON NEURO.

NOW, THE KEY HERE, WHAT YOU'RE ASKING US, IS WHAT'S THE STRATEGY. THE STRATEGY STARTED WITH THE NEURO TASK FORCE UNDERSTANDING THERE WAS NO FOCUS OR INVESTMENT IN NEUROPSYCHIATRIC DISORDERS. WE DID THE DISC4 REMIND-L FOCUS ON THAT. AND THEN NOW WHAT WE ARE BRINGING TO YOU TODAY USING THAT

SAME MODEL IS A SERIES OF PROGRAMS. THIS ONE DOES NOT HAVE FOCUS, BUT THE NEXT ONE HAS THE POSSIBILITY FOR FOCUS. SO WE COULD HAVE THAT DISCUSSION AFTER CHAN'S PRESENTATION, AND I THINK THAT MIGHT BE A PLACE WHERE THE BOARD AND THE NEURO TASK FORCE DECIDES THEY WANT TO HAVE MORE OF A SAY IN THE FOCUS. THAT'S WHAT I COULD SUGGEST.

DR. LEVITT: OKAY. IF IT'S GOING TO BE TAKEN UP IN THAT WAY, I'M FINE WITH THAT. I DON'T WANT TO DELAY ANYTHING BECAUSE I THINK THE APPROACHES, WHICH ARE A MIRROR FOR WHAT WAS DONE WITH THE REMIND, BOTH THE L AND THE REMIND-L AND THE REMIND WHATEVER THE OTHER LETTER IS. BUT IT'S BASICALLY THE SAME PROGRAMS, AND THEY WORK REALLY WELL. AND YOU MENTIONED IT ALREADY. NEURO AS A CATCHALL IS THE MOST DIVERSE AREA OF INVESTIGATION BECAUSE IT GOES EVERYTHING FROM ONCOLOGY TO METABOLISM. AND IT'S ENORMOUS.

AND SO I GET THAT WE'RE GOING TO MEET THE GOALS OF 1.4 BILLION, BUT THE TASK FORCE IDENTIFIED CERTAIN AREAS THAT WERE WAY UNDERINVESTED. AND THAT'S WHAT I'M MOST CONCERNED ABOUT. SO IF WE TAKE IT UP LATER, I'M FINE WITH THAT AS LONG AS IT'S ON THE AGENDA, WE TAKE IT UP, AND WE'RE SERIOUS ABOUT TRYING TO ADDRESS THE DEFICIENCIES IN SPECIFIC

AREAS, INCLUDING THOSE THAT WERE CALLED OUT IN PROPOSITION 14, BY THE WAY, SO NOT MY LANGUAGE. IT WAS IN THE PROP. OKAY?

DR. CANET-AVILES: ABSOLUTELY. THANK YOU, PAT, FOR THE POINT.

ONE MORE POINT I FORGOT TO MENTION IS THAT PART OF WHAT WAS STARTED WITH THE MODEL OF THE NEURO TASK FORCE HAS NOW BEEN EXTENDED TO THIS PREFERENCE-SETTING EXERCISE. FOR THE PURPOSE OF THIS YEAR, BECAUSE OF THE PASSING OF THE TIME, WE ARE PRESENTING IT IN TWO PARTS. HALF OF IT IS IMPLEMENTED IN THE CONTEXT OF THE CONCEPT PRESENTATION. THE OTHER HALF WILL COME IN JUNE WHEN WE PROVIDE THE FORMALIZED PORTFOLIO PERFORMANCE REVIEW AND A COMPREHENSIVE ASSESSMENT OF WHERE ARE WE WITH AWARDS AND WHAT ARE THE CURRENT GAPS WITH THE LANDSCAPE AS WELL. AND THE BOARD, THE NEURO TASK FORCE, AND SCIENCE SUBCOMMITTEE WILL HAVE A CHANCE TO REVIEW PROPOSED ADJUSTMENTS TO FUNDING PRIORITIES WHICH WOULD THEN BE INCORPORATED INTO THE NEXT CYCLES OF OUR PROGRAM ANNOUNCEMENTS.

SO I THINK YOU ARE RIGHT ON THE SPOT AS ALWAYS, AND WE REALLY APPRECIATE WHAT YOU ARE SAYING. AND I HOPE THAT IN THE NEXT PRESENTATION THERE IS A BIT OF A CHANCE TO DISCUSS THAT FOCUS.

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DR. LEVITT: THAT SOUNDS GREAT. THANKS, ROSA.

MR. TOCHER: JUDY GASSON.

DR. GASSON: THANK YOU VERY MUCH. AND I ENDORSE WHAT PAT JUST SAID, BUT I HAD A SLIGHTLY DIFFERENT QUESTION. AND COULD YOU, FOR THE BENEFIT OF FOLKS THAT ARE NEW TO THIS COMMITTEE OR MEMBERS OF THE PUBLIC, CAN YOU REMIND US HOW THE TWO-STEP REVIEW PROCESS WORKS PLEASE?

DR. SHEPARD: YES, I CAN.

DR. GASSON: THANK YOU.

DR. SHEPARD: SO THE WAY IT WORKS IS THAT APPLICANTS WILL SUBMIT A FULL APPLICATION AND CIRM WILL RECEIVE THEM ALL. AND IF IT EXCEEDS A CERTAIN NUMBER, THEN THIS TWO-STEP PROCESS KICKS IN. AND THE FIRST STEP IS A STEP CALLED POSITIVE SELECTION. SO WHAT HAPPENS IS THE APPLICATIONS ARE PUT INTO A POOL THAT ARE THEN VIEWED BY MEMBERS OF THE GRANTS WORKING GROUP WHO WILL GO THROUGH AND LOOK AT THEM, AND THEY WILL EACH BE GIVEN A CERTAIN NUMBER OF CHOICES TO MAKE SELECTIONS. THOSE CHOICES ARE THEN FORWARDED TO THE SECOND STAGE OF REVIEW, WHICH IS THE TRADITIONAL GWG REVIEW WHERE THERE'S A FULL SET OF DISCUSSION AND COMMENTS AND CRITIQUES AND SCORES.

SO APPLICATIONS THAT DON'T MAKE IT THROUGH

THAT FIRST STEP ARE DEEMED TO BE DENIED. THEY DON'T RECEIVE A SCORE. BUT THOSE THAT MAKE IT THROUGH TO THE SECOND STAGE DO RECEIVE A SCORE AND CRITIQUES THAT THEY CAN ADDRESS IF THEY CONSIDER APPLYING WITH A SIMILAR PROJECT IN THE FUTURE EDITION OF THE PROGRAM.

THERE'S ALSO A STEP WHERE PATIENT ADVOCATE MEMBERS OF CIRM'S GOVERNING BOARD CAN MAKE SELECTIONS DURING THE FIRST PHASE OF REVIEW. SO THEY CAN ADD SOME TO THE POOL. AND THE CIRM STAFF HAS A ROLE TO LOOK THROUGH ANYTHING THAT WASN'T SELECTED TO MAKE SURE THAT THERE ISN'T ANYTHING HIGHLY IMPACTFUL OR MERITORIOUS THAT MIGHT HAVE BEEN OVERLOOKED THAT MIGHT ALSO BE ABLE TO BE REVIEWED IN THAT POOL.

CHAIRMAN FISCHER-COLBRIE: WITH THAT, IF WE MIGHT -- OH, I'M SORRY, JUDY. I'M SORRY. GO AHEAD.

MR. TOCHER: NO, MARK. I THINK THAT WAS INTERNAL HERE IN THE ROOM.

CHAIRMAN FISCHER-COLBRIE: OH, SORRY ABOUT THAT. ANY ADDITIONAL -- IF THERE ARE NO ADDITIONAL COMMENTS OR QUESTIONS, WE CAN MOVE TO THE MOTION, GET A MOTION FROM THE COMMITTEE.

DR. SOUTHARD: MOVE APPROVAL.

VICE CHAIR BONNEVILLE: SECOND.

MR. TOCHER: OKAY. WE HAVE A MOTION TO APPROVE -- RECOMMEND APPROVAL TO THE BOARD FROM MARV SOUTHARD, SECONDED BY MARIA BONNEVILLE.

CHAIRMAN FISCHER-COLBRIE: GREAT. JUST TO CLOSE IT OUT, ANY OTHER COMMENTS OR QUESTIONS FROM THE COMMITTEE BEFORE WE ASK THE PUBLIC?

MR. TOCHER: I DON'T SEE ANY.

CHAIRMAN FISCHER-COLBRIE: NOTHING?

MR. TOCHER: CORRECT.

CHAIRMAN FISCHER-COLBRIE: OKAY. AND THEN WE CAN ASK ANYTHING FROM THE PUBLIC IN TERMS OF QUESTIONS OR COMMENTS.

MR. TOCHER: FROM THE PUBLIC, WE'RE LOOKING. I DON'T SEE ANY. NO. IT APPEARS NO COMMENT FROM THE PUBLIC.

CHAIRMAN FISCHER-COLBRIE: OKAY. WITH THAT, LET'S GO AHEAD WITH THE ROLL CALL ROTE.

MR. TOCHER: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

MR. TOCHER: LEONDRA CLARK-HARVE.

DR. CLARK-HARVEY: YES.

MR. TOCHER: DEBORAH DEAS.

DR. DEAS: YES.

MR. TOCHER: MARK FISCHER-COLBRIE.

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CHAIRMAN FISCHER-COLBRIE: YES.
MR. TOCHER: ELENA FLOWERS.
DR. FLOWERS: YES.
MR. TOCHER: JUDY GASSON.
DR. GASSON: YES.
MR. TOCHER: JEFF GOLDEN.
DR. GOLDEN: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: YES.
MR. TOCHER: PAT LEVITT.
DR. LEVITT: YES.
MR. TOCHER: CAROLYN MELTZER.
DR. MELTZER: YES.
MR. TOCHER: CHRIS MIASKOWSKI.
DR. MIASKOWSKI: YES.
MR. TOCHER: MARV SOUTHARD.
DR. SOUTHARD: YES.
MR. TOCHER: KAROL WATSON.
DR. WATSON: YES.
MR. TOCHER: KEITH YAMAMOTO.
DR. YAMAMOTO: YES.
MR. TOCHER: THANKS VERY MUCH. THE MOTION CARRIES UNANIMOUSLY.

DR. SHEPARD: THANK YOU, EVERYONE.

CHAIRMAN FISCHER-COLBRIE: LET'S GET ON TO THE NEXT DISCUSSION. THANK YOU.

DR. LEK TAN: HI. THANK YOU, KELLY. AND GOOD AFTERNOON TO MEMBERS OF THE BOARD. MY NAME IS CHAN LEK TAN. AND FOR THE NEXT SECTION, I WILL PROVIDE AN OUTLINE OF THE AMENDMENTS TO THE DISCOVERY4 CONCEPT.

AGAIN, WE WILL USE THE SAME OUTLINE STARTING WITH THE BACKGROUND TO THE CONCEPT COVERING THE HIGH LEVEL OVERVIEW OF KEY ELEMENTS OF THE AWARD STRUCTURE, AND WE'LL END WITH A TIMELINE AND A REQUEST FOR A MOTION TO RECOMMEND.

JUST A QUICK REMINDER AGAIN THAT BOTH DISCOVERY CONCEPTS ARE GUIDED BY GOAL 1 AND THE CORRESPONDING RECOMMENDATION TO SUPPORT COMPREHENSIVE DISCOVERY RESEARCH THROUGH THESE TWO FUNDING STRUCTURES. THE GOAL IS TO PROVIDE SCIENTIFIC FINDINGS THAT WILL LAY THE FOUNDATION FOR FUTURE THERAPEUTIC DEVELOPMENT, INCLUDING THROUGH FUTURE PRECLINICAL DEVELOPMENT AT CIRM.

AS KELLY HAS DESCRIBED, WE HAVE ARTICULATED A SIMPLE, COMMON OBJECTIVE FOR BOTH DISC4 AND DISC5 BASED ON THE RECOMMENDATION ITSELF. THE APPROACH THAT DISC4 CONCEPTS WILL TAKE IS ONE

THAT IS COMPLEMENTARY TO WHAT YOU HAVE JUST HEARD HAD FROM KELLY FOR DISC5.

DISC4 BUILDS ON THE REMIND PROGRAM TO SUPPORT LARGE, COLLABORATIVE TEAMS THAT HAVE EXPANSIVE STUDIES THAT INTEGRATE MULTIPLE DISCIPLINES AND APPROACHES WITH A FOCUS ON DISCOVERY OF -- WITH A FOCUS ON DISEASE BIOLOGY IN ORDER TO FACILITATE TARGET AND BIOMARKER IDENTIFICATION.

ONCE AGAIN, BOTH DISCOVERY PROGRAMS WILL MAKE IT EASIER FOR PROGRAM INFRASTRUCTURE, SOME OF WHICH ARE BEING PILOTED RIGHT NOW WITH THE REMIND PROGRAM, INCLUDING GRANTEE MEETINGS, DATA SHARING INFRASTRUCTURE, AND POTENTIAL TO LEVERAGE INTERNAL AND EXTERNAL PARTNERSHIPS TO INCREASE SCIENTIFIC IMPACT AND THE POTENTIAL FOR TRANSLATION.

AND JUST TO RETURN TO THE FOCUS ON DISC4, THE RATIONALE BEHIND THIS PROGRAM AND THE REMIND PROGRAM BEFORE THIS IS THAT, DESPITE THE NEW THERAPEUTIC PLATFORMS AND MODALITIES, SOUND TARGETS BASED ON STRONG BIOLOGICAL UNDERSTANDING REMAINS ONE OF THE MOST IMPORTANT BOTTLENECKS TO TREATMENTS. LARGELY THIS IS DUE TO THE COMPLEXITY OF DISEASE BIOLOGY. SO THE TEAM AND THE BOARD ACKNOWLEDGES THAT APPROACHES THAT INTEGRATE THINGS FROM MULTIPLE DISCIPLINES AND COMPLEMENTARY APPROACHES IS THE KEY

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TO SUCCESS HERE.

DISC4 WILL APPLY THIS MULTIDISCIPLINARY APPROACH TO THE UNDERSTANDING OF DISEASE BIOLOGY. PROPOSALS MUST AIM TO ACHIEVE ONE OR MORE OF THE FOLLOWING OUTCOMES. BETTER UNDERSTANDING OF HUMAN DISEASE BIOLOGY THROUGH NOVEL MECHANISTIC INSIGHTS. EXTENDING OUR UNDERSTANDING OF DISEASE MECHANISMS TO DIVERSE HUMAN POPULATIONS. AND ULTIMATELY IDENTIFYING AND VALIDATING NOVEL THERAPEUTIC TARGETS, STRATEGIES, AND/OR BIOMARKERS.

AND AS YOU'VE HEARD, DISC4 BUILDS ON THE FRAMEWORK THAT WE PILOTED THROUGH THE REMIND PROGRAM, SPECIFICALLY THE REMIND-L AWARD THAT HAD A FOCUS ON NEUROPSYCHIATRIC DISORDERS SUCH AS SCHIZOPHRENIA AND AUTISM.

AND THE TWO MAJOR CHANGES THAT WE ENVISION HERE GOING FROM REMIND TO DISC4 IS, FIRST, THE EXPANSION OF THE SCOPE TO SUPPORT NOT JUST OTHER DISEASE AREAS, BUT ALSO TO TAKE A SYSTEMS BIOLOGY APPROACH THAT HAS THE POTENTIAL TO ALLOW TEAMS TO CUT ACROSS DISEASE -- TRADITIONAL SILOS AS WELL AS DISEASE INDICATIONS.

THE SECOND SET OF CHANGES SEEKS TO BETTER POSITION TEAMS FOR READINESS FOR TARGET VALIDATION BY THE END OF THE AWARD PERIOD. WE DON'T WANT TO BE

DETRACTING FROM THE CORE FOCUS ON DISEASE BIOLOGY INSIGHTS SO THAT NEW DISCOVERIES CAN BE MORE RAPIDLY TRANSLATED INTO PRECLINICAL EFFORTS. AND THIS IS IMPLEMENTED THROUGH A SERIES OF SMALLER CHANGES ACROSS THE PROGRAM DESIGN, MANY OF WHICH WILL NOT BE TOUCHED UPON TODAY, BUT WOULD INCLUDE THINGS LIKE THE APPLICATION MATERIALS, THE REVIEW PROCESS, AND BOARD MANAGEMENT.

SO THIS SLIDE SUMMARIZES ALL THE MAJOR ELEMENTS OF THE AWARD STRUCTURE. MUCH OF IT IS PRESERVED FROM THE REMIND PROGRAM. IN BOLD ARE THE ELEMENTS WHERE THE CHANGES HAVE BEEN MADE, AND WE WILL SAY MORE ABOUT EACH OF THOSE IN TURN IN A BIT.

JUST TO RECAP, THIS IS A FOUR-YEAR AWARD FOR TEAMS OF FIVE OR MORE CALIFORNIA-BASED INVESTIGATORS WITH ONE CONTACT PI AND AT LEAST FOUR CO-INVESTIGATORS. THE BASE BUDGET IS FOR $13 MILLION IN TOTAL COSTS, AND WE EXPECT TO FUND SIX TEAMS A YEAR FOR AN ANNUAL BUDGET OF $84 MILLION.

AND JUST TO GO INTO THE AWARD BUDGET A LITTLE BIT MORE, THESE AWARD BUDGETS ARE CAPPED AT A BASE OF $13 MILLION IN TOTAL COST INCLUSIVE OF OVERHEADS. IN ALIGNMENT WITH DISC5, WE ARE ALSO MOVING FROM A DIRECT COST CAP IN THE REMIND PROGRAM TO NOW A TOTAL COST CAP TO ALIGN BOTH WITH DISCOVERY

AND ACROSS CIRM MORE BROADLY AND HAS THE IMPORTANT SIDE EFFECTS OF REMOVING DISINCENTIVES FOR MULTI-INSTITUTIONAL TEAMS. SO WE GET TO THIS NUMBER BY APPLYING THE SAME DIRECT COST CAP TO REMIND AT $8 MILLION AND APPLYING A 62-PERCENT OVERHEAD RATE, WHICH IS JUST ABOVE THE ACTUAL AVERAGE OVERHEAD RATES OF 60 PERCENT HISTORICALLY.

SIMILAR TO REMIND, AN ADDITIONAL $1 MILLION IN TOTAL COST CAN BE REQUESTED WITH THE CONTRIBUTION OF ELIGIBLE MATCHING FUNDS OF EQUAL OR GREATER VALUE.

SO ELIGIBLE PROJECTS IN THIS AWARD MUST ADDRESS KNOWLEDGE GAPS OR BOTTLENECKS IN THE UNDERSTANDING OF HUMAN DISEASES. TO ENSURE ALIGNMENT WITH CIRM'S MISSION, THE OVERALL PROJECT MUST ALSO INCLUDE STUDIES THAT EMPLOY HUMAN STEM CELLS AND/OR GENETIC RESEARCH AS PART OF THE CENTRAL APPROACH OR HYPOTHESIS. ALTHOUGH, GIVEN THE STRUCTURE OF THE PROGRAM, APPLICANTS ARE ENCOURAGED TO INTEGRATE A VARIETY OF APPROACHES, MODELS, AND TECHNOLOGIES TO MAXIMIZE SCIENTIFIC IMPACT.

AND AS WITH ALL OUR PROGRAMS, THESE AWARDS MUST BE CENTERED ON HUMAN BIOLOGY AND EMPLOY HUMAN-DERIVED CELLS, TISSUES WHERE POSSIBLE. APPLICANTS MAY INCLUDE NONHUMAN MODELS TO ACHIEVE

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SPECIFIC OBJECTIVES, BUT MUST, IN TURN, PROVIDE STRONG JUSTIFICATION FOR ANY SUCH USE OF NONHUMAN MODELS.

THE AWARD IS OPEN TO CALIFORNIA-BASED NON-PROFIT OR FOR-PROFIT ORGANIZATIONS. EACH TEAM HAS A SCIENTIFIC LEADERSHIP OF WHAT WE CALL A CORE TEAM WITH A MINIMUM OF FIVE INVESTIGATORS, A CONTACT PI, AND FOUR OR MORE CO-INVESTIGATORS.

IN CONTRAST TO REMIND, WE ARE ALSO REQUIRING AT LEAST ONE MEMBER OF THE CORE TEAM TO COME FROM INSIDE OF THE PI INSTITUTION.

THE BROADER TEAM, WHICH INCLUDES KEY PERSONS IN ADDITION TO THE CORE TEAM, MUST INCLUDE ONE MEMBER OF EACH WITH THE RELEVANT CLINICAL, COMPUTATIONAL, AND INDUSTRY AND TRANSLATIONAL EXPERTISE AS WELL. IN ADDITION, ALL TEAMS MUST HAVE A DATA PROJECT MANAGER THAT WILL WORK WITH CIRM TO ENSURE DATA SHARING VIA REPORTING. WE HAVE A 15-PERCENT AND 10-PERCENT EFFORT MINIMUM FOR THE INVESTIGATORS AND THAT IS UNCHANGED.

SO AN IMPORTANT CHALLENGE THAT WE FACE WITH EXPANDING THE SCOPE FROM REMIND WHICH HAD A NARROW FOCUS ON NEUROPSYCHIATRIC DISEASES TO AN OPPORTUNITY THAT'S AVAILABLE TO RESEARCHERS ACROSS ALL DISEASE AREAS AS WELL AS RESEARCH THAT CUTS

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ACROSS DISEASE INDICATIONS. THIS INVOLVED A BALANCE OF SEVERAL FACTORS, NOT LEAST OF ALL THE POTENTIAL FOR HIGH APPLICATION VOLUMES. AND WE NEED TO ENSURE THAT REVIEW PANELS WITH SUFFICIENTLY FOCUSED EXPERTISE. AND MORE IMPORTANTLY WE WANTED TO PRESERVE MANY OF THE KEY ADVANTAGES AND POTENTIAL FOR IMPACT THAT WERE PRESENT WITH THE MORE FOCUSED APPROACH.

SO IN LIGHT OF THESE CONSIDERATIONS AND FOLLOWING BOARD MEMBER FEEDBACK, THE DISC4 AWARD WILL BE OPEN TO ALL ELIGIBLE APPLICATIONS WITHOUT RESTRICTIONS IN TOPIC OR DISEASE. SO PARTICULARLY EXCITING OR IMPACTFUL PROPOSALS WILL FIND A CHANCE TO BE REVIEWED IN ANY CYCLE.

IN ADDITION, WE PROPOSE THAT SELECT RESEARCH TOPICS BE PRIORITIZED EACH YEAR. AND THIS PROCESS WILL TAKE THE FOLLOWING FORM. CIRM TEAM WILL PRESENT RECOMMENDATIONS TO THE SCIENCE SUBCOMMITTEE FOR FUNDING PREFERENCES ANNUALLY. AND WE'LL GIVE YOU SOME OF THOSE RECOMMENDATIONS ON THE NEXT SLIDE. AND THIS COMMITTEE WILL THEN BE SENDING THOSE RECOMMENDATIONS TO THE ICOC FOR APPROVAL, AND THOSE PREFERENCE TOPICS WILL BE INCORPORATED INTO THE PROGRAM ANNOUNCEMENT FOR THE SUBSEQUENT CYCLE.

THIS WILL ALLOW US TO MAXIMIZE THE

POTENTIAL FOR SYNERGY ACROSS TEAMS AS WE HAD FOR REMIND. INCREASE THE POTENTIAL TO LEVERAGE COMMON EXTERNAL PARTNERSHIPS. AND CAPITALIZE ON OPPORTUNITIES IN THE EVOLVING RESEARCH LANDSCAPE AND ADDRESS POTENTIAL PORTFOLIO GAPS AS WELL.

SO FOR THIS FIRST CYCLE, THE TEAM HAS CONSIDERED A BROAD SET OF PREFERRED TOPICS AS SHOWN HERE. THIS IS SIMILAR -- WE HAVE TAKEN A PROCESS THAT IS SIMILAR TO THE SELECTION OF NEUROPSYCHIATRIC DISEASES -- THAT LED TO THE SELECTION OF NEUROPSYCHIATRIC DISEASES AS THE PILOT FOCUS AREA BY THE NEUROSCIENCE TASK FORCE. AND THESE ARE CONSIDERED A RELATIVE REPRESENTATION OF THESE TOPICS IN OUR EXISTING PORTFOLIO, THE RELEVANCE OF THESE TOPICS TO DISEASES OF HIGH UNMET NEED AND BURDEN, AND OPPORTUNITIES FOR LEVERAGING NEW ADVANCES IN STEM CELL MODELS.

SO I WON'T READ ALL THE TOPICS THAT WE'VE CONSIDERED. BUT FOR THIS NEXT CYCLE, CIRM STAFF RECOMMENDS TO INCLUDE A PREFERENCE FOR APPLICATIONS INVESTIGATING THE FIRST CATEGORY SHOWN HERE, THAT OF METABOLIC PHYSIOLOGY, THE INFLUENCE OF DIET OR MICROBIOME ON DISEASE BIOLOGY AND HEALTH, AND APPLICATIONS THAT SEEK TO UNDERSTAND THE BIOLOGY OF THE GI TRACT, LIVER, KIDNEY, PANCREAS, OR ENDOCRINE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

ORGANS, INCLUDING ADIPOSE TISSUE.

SO WE CAME TO THIS RECOMMENDATION FOR A NUMBER OF REASONS. FIRST, THIS TOPIC HAS LOWER REPRESENTATION IN CIRM'S PORTFOLIO THAN OTHER TOPICS SHOWN HERE. ALTHOUGH THIS AWARD WILL CUT ACROSS DISEASE TYPES, SOME OF THE MOST RELEVANT DISEASES IN THIS AREA INCLUDE HYBRID INDICATIONS LIKE DIABETES, FATTY LIVER DISEASE. AND AS DATA EMERGES FROM SOME OF THE MORE WELL-KNOWN DRUG INDICATIONS NOW AND THE EFFECTS ON OBESITY AND METABOLIC SYNDROME, THERE MIGHT BE A POSSIBILITY THAT UNDERSTANDING THESE AREAS WOULD HAVE A BROADER IMPACT ON OTHER DISEASE AREAS AS WELL.

AND FINALLY, WE WANTED TO HIGHLIGHT THAT THIS PARTICULAR RESEARCH TOPIC AREA, WE EXPECT TO HAVE A SLIGHTLY LOWER APPLICATION VOLUME COMPARED TO THE OTHER TOPICS SHOWN HERE WHICH WOULD ALSO ALLOW US TO PILOT OUR NEW FRAMEWORK AND TO TROUBLESHOOT SOME OF OUR INTERNAL PROCESSES AS WELL.

SO SIMILAR TO THE REMIND -- TO SOME PROGRAMS IN THE PAST AND THE CONCEPTS THAT YOU WILL HEAR ABOUT LATER TODAY, THIS PROGRAM WILL IMPLEMENT A PRESUBMISSION PROCESS TO ENSURE THAT APPLICATIONS ALIGN WITH PROGRAM SCOPE, OBJECTIVES, AND HELP US PRIORITIZE PROPOSALS IN THE CHOSEN PREFERENCE TOPIC

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

AREA.

THIS PROCESS WILL ALSO REDUCE TIME BURDEN FOR APPLICANTS, ESPECIALLY THOSE WITH POOR FIT FOR THIS PROGRAM WHILE THE EXTENDED TIMELINE, WE HOPE, WILL ALSO ALLOW APPLICANTS TO FORM NEW COLLABORATIONS THAT COULD LEAD TO MORE IMPACTFUL PROPOSALS.

AND FINALLY, THIS WOULD ALSO GIVE US THE FLEXIBILITY TO MANAGE HIGH APPLICATION VOLUMES AND PREPLAN FOR THE APPROPRIATE REVIEW PANEL WHERE WE NEED THEIR EXPERTISE.

IN ADDITION, DISC4 WILL ALIGN WITH DISC5 AND OTHER CIRM PROGRAMS TO MAKE CHANGES TO THE SCORING SYSTEM, MOVING TO A 1 TO 100 NUMERICAL SCORING SYSTEM AND OTHER CHANGES IN THE REVIEW PROCESS THAT WILL INCREASE THE VISIBILITY OF SCORE-DRIVING DECISIONS.

WE CONTINUE TO REQUIRE DATA SHARING AND MANAGEMENT PLAN AND COORDINATION WITH CIRM'S DATA INITIATIVES. THAT IS UNCHANGED FROM WHAT WE HAVE RIGHT NOW WITH REMIND.

AND WITH THE APPROVAL WE CAN QUICKLY MOVE TO POST THE PA BY EARLY APRIL WITH AN EXPECTATION FOR PRESUBMISSIONS DUE IN JUNE.

AND WITH THE REQUEST FOR MOTION TO

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

RECOMMEND APPROVAL TO THE FULL ICOC FOR THIS DISC4 CONCEPT AND HAPPY TO TAKE QUESTIONS AS WELL.

CHAIRMAN FISCHER-COLBRIE: LET'S GO AHEAD AND GET THE MOTION ON THE TABLE. THEN WE CAN MOVE INTO THE DISCUSSION. SO WITH THAT, I'M CALLING FOR A MOTION AND A SECOND.

DR. MELTZER: MOTION TO APPROVE.

DR. SOUTHARD: SECOND.

CHAIRMAN FISCHER-COLBRIE: THANK YOU. AND WITH THAT, LET'S OPEN UP FOR QUESTIONS AND DISCUSSION.

MR. TOCHER: LOOKS LIKE JUDY GASSON --

DR. LEVITT: MAYBE YOU CAN ELABORATE A LITTLE BIT MORE ON THE DOMAINS WHERE YOU SAID THERE WAS A RED X BECAUSE SOME OF THE THINGS LISTED THERE LIKE THE GI SYSTEM, I KNOW THERE'S BEEN MULTIPLE GRANTS IN THAT AREA FOR SURE. IT WAS A LONG LIST. SO I'M JUST WONDERING, MAYBE YOU CAN ELABORATE BECAUSE THAT ONE WAS HIGHLIGHTED IN TERMS OF PREFERENCE.

DR. LEK TAN: YEAH. I CAN DEFINITELY GO INTO THAT. THIS RED DOT HERE SHOWING THE RELATIVE REPRESENTATION IN CIRM'S PORTFOLIO ACTUALLY COMBINES MULTIPLE DIFFERENT NUMBERS HERE. SO WE START BETWEEN THE DISC-0 AWARDS. IF YOU SUM UP THE AWARDS

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

WITHIN THE DISC-0 HISTORICALLY FOR THIS PARTICULAR BUCKET, IT COMES IN LAST OUT OF THE FIVE WITH THE BRAIN BIOLOGY AND IMMUNE AND BLOOD CATEGORIES BEING THE HIGHEST FOLLOWED BY CARDIOVASCULAR AND REPRODUCTION.

IF WE LOOK AT ACTIVE DISC2, TRAN, AND CLIN AWARDS, THIS AREA AROUND METABOLISM AND GASTROINTESTINAL BIOLOGY COMES IN JUST SECOND TO LAST, WHICH IS ONLY HIGHER THAN THE CARDIOVASCULAR BUCKET.

IN TERMS OF TOTAL FUNDING HISTORICALLY FROM 2015 TO 2024 ACROSS ALL OF OUR PROGRAMS, THIS PARTICULAR BUCKET FOR DIGESTIVE SYSTEM AND ENDOCRINE ALSO COMES IN SECOND TO LAST, ONLY SLIGHTLY HIGHER THAN THE CARDIOVASCULAR AS WELL.

IN TERMS OF RELEVANCE TO DISEASE --

DR. LEVITT: SO IT'S LESS REPRESENTED THAN PSYCHIATRIC DISORDERS?

DR. LEK TAN: PSYCHIATRIC DISORDERS, WE DIDN'T BREAK OUT THOSE NUMBERS SPECIFICALLY BECAUSE THEY'RE A SUBSET OF THE BROADER NEURO PROGRAM.

DR. LEVITT: ALL RIGHT.

DR. CANET-AVILES: WE COMPARE ACTUALLY TO NEURODEGENERATIVE, NOT NEUROPSYCHIATRIC, IN TERMS OF THE PREFERENCE TOPICS.

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

MR. TOCHER: JUDY GASSON.

DR. GASSON: TWO QUESTIONS. THE FIRST QUESTION IS IN THE TWO-STEP REVIEW PROCESS, AGAIN, IF I UNDERSTOOD YOU CORRECTLY, YOU'RE NOT SUBMITTING THE FULL GRANT APPLICATION FOR THE FIRST STEP; IS THAT CORRECT?

DR. LEK TAN: YES, THAT'S RIGHT. WE PROBABLY WON'T GO INTO THE DETAILS OF THE PRESUBMISSION PROCESS HERE. BUT JUST ON A HIGH LEVEL, THE PRESUBMISSION PROCESS WILL BE A MUCH SMALLER PRESUBMISSION PROPOSAL.

DR. GASSON: GREAT. OKAY. THAT'S GREAT.

BUT MY SECOND QUESTION WAS THE PREFERENCE. SO I'M WONDERING IF IT DOESN'T ALIGN WITH THE PREFERENCE, HOW WOULD A REALLY GREAT POTENTIALLY TRANSFORMATIVE PROJECT BE SELECTED IF IT DOESN'T, FOR WHATEVER REASON, ALIGN WITH THE CURRENT PREFERENCES?

DR. LEK TAN: YEAH. SO OUR THINKING RIGHT NOW IS THAT THE PREFERENCE TOPICS WILL BE ADJUDICATED THROUGH THE PRESUBMISSION PROCESS. AND THAT NEEDS TO BE WORKED OUT IN ITS DETAILS, WHETHER WE HAVE A FIRM KIND OF SCORING AND WEIGHTING SYSTEM, BUT WE WILL BE ABLE TO BALANCE THOSE TWO OUTCOMES HAVING THOSE PRIORITIZATION TOPICS BE WELL

REPRESENTED, BUT KEEPING THE FLEXIBILITY AND THE OPENNESS FOR OTHER PROPOSALS THAT ARE NOT WITHIN THOSE TOPICS, BUT SCORE HIGHLY IN TERMS OF ALIGNMENT TO OUR OBJECTIVES AND SCOPE AS WELL.

DR. GASSON: AND ARE YOU ENVISIONING THAT THAT WILL ALSO BE DONE BY THE GWG AT THAT POINT IN TIME?

DR. LEK TAN: I THINK I'LL REFER TO GIL ON THAT TOPIC.

DR. CANET-AVILES: DR. SAMBRANO IS ACTUALLY PREPARING A PRESENTATION FOR THE MARCH 27TH THAT WILL PREVIEW AND REVIEW PROCESSES. THIS PROCESS IS NOT PLANNED TO BE AT THE GRANTS WORKING GROUP, RIGHT, GIL; BUT HE IS GOING TO PRESENT FULLY ON THIS.

DR. SAMBRANO: CORRECT. YES, I'M GOING TO PROVIDE AN OVERVIEW THAT WILL HELP THE BOARD UNDERSTAND HOW WE ARE ALIGNING THE REVIEW WITH EACH OF THESE CONCEPTS AND THE OBJECTIVES OF EACH. AND WHAT IS BEING DESCRIBED HERE IS A PROCESS THAT INVOLVES, AS DESCRIBED, A PRESUBMISSION THAT IS REVIEWED BY THE CIRM PROGRAM TEAM TO DETERMINE THE ALIGNMENT WITH THE PROGRAM AND SELECT THE ONES THAT ARE BEST ALIGNED TO THEN MOVE FORWARD TO GWG. SO ESSENTIALLY THAT'S THE PROCESS.

THE MECHANISM THAT WE WILL USE IN ORDER TO ASSIGN POINTS OR MAKE SELECTIONS SO THAT WE CAN MAKE IT AS FAIR AND APPROPRIATE AS POSSIBLE IS PART OF WHAT WE WILL PRESENT IN MARCH.

DR. GASSON: GREAT. SO WE'LL TALK MORE ABOUT THIS IN MARCH. OKAY. THANK YOU.

MR. TOCHER: MARK AND THEN JEFF GOLDEN.

CHAIRMAN FISCHER-COLBRIE: YEAH. IF YOU CAN GO BACK TO THE PREVIOUS SLIDE ON THE PREFERENCES. CLEARLY THE GRAYED-OUT AREA WOULD BE INDICATIVE OF THE NEAR TERM PREFERENCE ELEMENT. TWO THINGS. ONE IS THIS THEN A SITUATION WHERE THERE'S A SOFT PREFERENCE BY SEQUENCE ON THE OTHER ONES, OR ARE THE NEXT FOUR BUCKETS INHERENTLY JUST MORE OR LESS RANDOM AND JUST USING THE DATA POINTS TO SHOW WHERE THEY'RE CHARACTERIZED, OR HOW ARE WE THINKING ABOUT THE OTHER FOUR ELEMENTS WITHIN THE FRAMEWORK OF THE FACT THAT WE'RE SAYING ANY APPLICATIONS ELIGIBLE FOR REVIEW, THIS IS OUR PREFERENCE?

DR. LEK TAN: THANK YOU FOR THAT QUESTION. I THINK WE ARE PRESENTING THESE FIVE OPTIONS HERE. THERE IS A SLIGHT RANKING IN TERMS OF HOW THE CIRM STAFF HAS SEEN WHICH ONES SHOULD RANK HIGHER, AND THEN WE ULTIMATELY TEND TO ALIGN ON METABOLIC PHYSIOLOGY AS OUR TOP CHOICE. BUT WITH THAT CHOICE,

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

ALL OTHER TOPICS WOULD STILL BE ELIGIBLE FOR SUBMISSION. AND WE WILL COME BACK TO THE BOARD EVERY YEAR WITH NEW RECOMMENDATIONS, AND SOME OF THESE WILL BE REPRODUCED IN THOSE SUBSEQUENT YEARS. AND THEN THE BOARD CAN MAKE A DECISION AGAIN.

DR. CANET-AVILES: AND JUST TO CLARIFY, THAT WAS THE TOP CHOICE FOR FY 25/26. AND THE REASON FOR THAT IS BECAUSE WE DID NOT -- WE ARE GOING TO BE PILOTING A PRESUBMISSION OR PREREVIEW PROCESS. AND WE THINK THAT WE WILL BE ABLE TO HANDLE THE NUMBER OF PREAPPLICATIONS WITH A TOPIC THAT MIGHT NOT BE AS MUCH DEMAND NOW. OKAY. JUST GOING TO STOP.

CHAIRMAN FISCHER-COLBRIE: OKAY. WELL, THANK YOU. THAT'S VERY HELPFUL. AND, AGAIN, THE LEAD-OFF ON THE PRESENTATION WITH RESPECT TO THE FACT THAT, EVEN THOUGH THERE ARE INDICATIONS AROUND A PREFERENCE FOR THE NEXT CERTAIN TIME PERIOD, THIS IS OPEN TO EVERYTHING ALONG THE WAY, AND IT'S NOT FOR CLOSING OFF PROGRAMS THAT COULD BE INCREDIBLY IMPACTFUL. SO THANK YOU.

DR. LEK TAN: EXACTLY. THANK YOU.

MR. TOCHER: JEFF GOLDEN.

DR. GOLDEN: YEAH. THIS MAY BE A NAIVE QUESTION, AND THIS IS MY FIRST TIME PARTICIPATING.

SO I APOLOGIZE FOR THAT. BUT HOW DO YOU ENSURE THAT ALL THESE AREAS ALIGN WITH REGENERATIVE MEDICINE STEM CELL BIOLOGY AND GENE THERAPY, ET CETERA, STEM CELL THERAPY? BECAUSE A LOT OF THESE COULD BE SET UP WITH THINGS -- IT'S JUST NOT CLEAR TO ME WHERE THAT FITS IN. AND MAYBE THAT'S IN THE KIND OF INTRODUCTION TO THE DISC4, BUT I JUST HAVEN'T SEEN IT HERE, AND I JUST WONDER HOW YOU PUT THAT TOGETHER.

DR. LEK TAN: YEAH. I THINK I WOULD ANSWER THAT BY GOING BACK TO THE PAGE ON PROJECTS ELIGIBILITY, WHICH IS AN ELIGIBILITY REQUIREMENT FOR ALL PROJECTS REGARDLESS OF THE YEAR OR THE PREFERENCE TOPICS. SO EVERY PROPOSAL, IN ORDER TO ALIGN WITH OUR MISSION, MUST INCLUDE STUDIES THAT EMPLOY HUMAN STEM CELLS AND/OR GENETIC RESEARCH AS PART OF THE CENTRAL APPROACH.

GIVEN OUR EXPERIENCE WITH REMIND, THAT TURNS OUT TO BE IN ALMOST ALL CASES A VAST MAJORITY OF THE APPLICATIONS THEMSELVES, BUT WE DO ENCOURAGE THEM TO BRING IN OTHER APPROACHES AS WELL WHERE NECESSARY AND IMPACTFUL.

DR. GOLDEN: GOT IT. THANK YOU.

DR. CANET-AVILES: THAT WAS PART OF THE WHOLE THINKING PROCESS WHEN WE CAME WITH THE PILOT

FOR DISC4 REMIND-L TO LEVERAGE OTHER DISCIPLINES IN ORDER TO MAKE SURE THAT WE CAN ANSWER THESE QUESTIONS AND PROVIDE MORE POWER TO THESE STUDIES.

MR. TOCHER: PAT LEVITT.

DR. LEVITT: YEAH. SO WHEN AN RFA GOES OUT OR A PA GOES OUT, AT LEAST IN MY EXPERIENCE, INVESTIGATORS ARE QUITE LITERAL ABOUT HOW THEY INTERPRET THE WORDING. SO TO ME THIS JUST FEELS TOO SQUISHY. LIKE, THERE WILL BE A PREFERENCE, BUT IT'S NOT EXACTLY CLEAR TO ME, WHAT DOES IT EXACTLY MEAN? HOW IS THE WORDING GOING TO BE? THIS IS NOT INSIGNIFICANT BECAUSE IN THE INITIAL DESIGN OF THIS, WHICH WE SAW, THERE WAS GOING TO BE LIKE A PREFERENCE EACH YEAR, LIKE A SPECIFIC PREFERENCE EACH YEAR. THERE WILL BE A CALL FOR INVESTIGATIONS IN CARDIOVASCULAR AND THAT WOULD BE IT. AND THAT WAS NOT -- I DIDN'T HEAR ANYBODY SUPPORTING THAT.

SO THIS IS SORT OF A MODIFICATION OF THAT, BUT TO ME THERE'S JUST NOT ENOUGH -- I DON'T UNDERSTAND HOW THIS IS GOING TO BE ADJUDICATED OR HOW THIS IS GOING TO BE DESCRIBED TO INVESTIGATORS. IF THEY READ -- LIKE I COULD WRITE THIS SENTENCE SEVERAL WAYS. ONE WOULD BE TARGETED TO OFF-PUTTING THOSE WHO ARE NOT DOING RESEARCH IN A CERTAIN AREA, AND OTHERS WOULD BE A SENTENCE THAT WOULD REASSURE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

THAT THERE'S GOING TO BE PLENTY OF OPPORTUNITY IF THE GRANT IS GREAT TO BE SUCCESSFUL. THAT'S HOW INVESTIGATORS THINK.

AND SO MAYBE YOU'RE GOING TO DEAL WITH THIS, BUT I THINK IF IT COMES BACK TO THE BOARD HOW THIS WAS HANDLED AND IT WASN'T REALLY TRANSPARENT FOR INVESTIGATORS, I'LL JUST SPEAK FOR MYSELF, I'M NOT GOING TO BE REAL HAPPY ABOUT THAT BECAUSE WE HAVE TO BE REALLY TRANSPARENT WITH INVESTIGATORS. THEY'RE LITERAL ABOUT HOW THEY INTERPRET THESE THINGS. AND YOU ALL KNOW THIS FROM YOUR HISTORY OF HOW YOU'VE WORKED HERE. SO I JUST HAD TO SAY THAT. I JUST THINK THAT RIGHT NOW FOR US I DON'T KNOW IF SQUISHY IS AN OFFICIAL SCIENTIFIC TERM, MARK, BUT THAT'S HOW IT FEELS.

CHAIRMAN FISCHER-COLBRIE: I THINK, PAT, YOUR POINT IS WELL TAKEN BECAUSE THE ISSUE IS GOING TO BE A CONDITION OF DO I GO THROUGH THE EFFORT IN TIME TO FILE AN APPLICATION OR NOT, OR IS IT INHERENTLY GOING TO AUTOMATICALLY GET SHUT DOWN OR NEARLY SHUT DOWN. YOUR QUESTION IS VERY MUCH ON POINT HERE. SORRY TO INTERRUPT.

DR. LEVITT: I'M JUST SAYING I COULD WRITE THAT SENTENCE THREE DIFFERENT WAYS. I KNOW IT WOULD HAVE THREE DIFFERENT IMPACTS. SO THAT TO ME IS LIKE

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

HOW IS THIS SENTENCE GOING TO BE WRITTEN SO THAT EVERYONE IS ENCOURAGED, BUT WE'RE PARTICULARLY INTERESTED IN ATTRACTING IN A CERTAIN FIELD. SO IT'S GOT TO BE DONE REALLY CAREFULLY SO THAT WE DON'T OFF-PUT THOSE WHO ARE SAYING WHY AM I GOING TO SPEND THREE MONTHS PUTTING A GRANT TOGETHER WHERE THE ODDS ARE 1 IN 20; WHEREAS, IF I DID IT IN, LET'S SAY, SMALL INTESTINE, THE ODDS WOULD BE 1 IN 3. THAT'S HOW INVESTIGATORS LOOK AT THIS.

DR. CANET-AVILES: PAT, SO ACTUALLY THE PREFERENCE SETTING, AND I THOUGHT WE HAD IT HERE IN A FOOTNOTE, BUT THE PREFERENCE SETTING IS GOING TO BE WORKED OUT AT THE PREREVIEW PROCESS. SO THE APPLICANTS WILL NOT HAVE TO DO THE FULL APPLICATION, WHICH ARE VERY BURDENSOME. WE ARE GOING TO PROBABLY HAVE A VERY SMALL PREAPP WITH WHAT'S THE TOPIC, WHO ARE THE COLLABORATORS, AND THE DIFFERENT DISCIPLINES, AND A SERIES OF QUESTIONS SO WE CAN THEN INVITE LIKE WITH THE REVIEW IS GOING TO BE 30. THERE WILL BE 30 APPLICANTS, AND THEN AT THAT STAGE, WHEN THEY COME TO THE REVIEW, EVERYBODY IS AT THE SAME LEVEL OF PREFERENCE. THE PREFERENCE WILL NO LONGER BE THERE BECAUSE WE WILL HAVE ALREADY DECIDED THAT THOSE PEOPLE ARE ALL VALID TO BE COMING TO REVIEW. AND THEN THERE WILL BE OTHER CRITERIA THAT

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

WILL BE IN TERMS OF IMPACT AND FEASIBILITY, ET CETERA. RIGHT.

SO THE PREFERENCE, JUST TO BE CLEAR, COULD BE BEFORE WE ASK ANYBODY TO COME WITH A FULL REVIEW, A FULL APPLICATION.

NOW, ONE OF THE THINGS THAT WE HAVE DONE IS WE'VE -- SO DISEASES IN THE MOST LOGICAL SENSE, HUMAN DISEASES NOW CUTTING ACROSS SYSTEMS. AND WE'VE BEEN TRYING TO TAKE A SYSTEMS BIOLOGY APPROACH, IF YOU WANT TO GO TO THAT. SO IF WE THINK ABOUT SETTING PREFERENCE FOR THE METABOLIC PHYSIOLOGY, DIET, MICROBIOME, THERE'S A STRONG FOUNDATION FOR ALSO EXPLORING IF SOMEBODY WANTS TO TAKE THE HEAT THERE, THEY CAN COME AND SAY WE ARE EXPLORING NEURODEGENERATION, GUT/BRAIN ACCESS DISORDERS, LIVER-BRAIN INTERACTIONS, ET CETERA, THE NEURO COMPONENT CAN ALSO BE THERE. SO THERE'S A LOT OF CROSSTALK AMONGST THESE. WHAT WE'RE ASKING PEOPLE IS TO GIVE US A PREFERENCE FOCUS.

NOW, THE BOARD HAS THE PREROGATIVE TO SAY, LOOK, WE DON'T WANT YOU TO START WITH THAT OR WE DON'T WANT YOU TO START WITH THESE PREFERENCE TOPICS. WE WANT YOU TO DO IT DIFFERENTLY. OR WE WOULD LIKE FOR YOU TO COME IN WITH ALL COMERS EVERY YEAR AND SET THE PREFERENCE TO NEURO. AND EVERY

YEAR SAY THIS YEAR IS GOING TO BE NEURODEGENERATIVE, NEXT YEAR NEURODEVELOPMENTAL, THE OTHER YEARS NEUROPSYCHIATRIC. LIKE WE COULD DO SOMETHING LIKE THAT TO BE MORE COMPLIANT WITH WHAT YOU HAD ASKED BEFORE. RIGHT.

SO THERE ARE OPTIONS. THAT'S WHY WE THOUGHT A LOT ABOUT DIFFERENT OPTIONS. WE CAME WITH THIS OPTION TO THE BOARD, BUT WE ARE HAPPY TO TAKE FEEDBACK AND COME IN WITH SOMETHING LATER. I'M JUST AWARE THAT THERE IS A LOT OF NEED FOR FUNDING AND TO KEEP THIS GOING. AND WE ALSO UNDERSTAND THAT WE WANT TO MAXIMIZE THE LEVERAGING OF DATA FOR NEURO. SO WE ARE HERE TO HEAR YOUR FEEDBACK.

DR. LEVITT: YEAH. LISTEN, I'M NOT -- I'VE WORKED ON THE GASTROINTESTINAL SYSTEM. SO I LOVE THE GASTROINTESTINAL SYSTEM. I LOVE BIOGASTROINTESTINAL SYSTEMS. SO THAT'S NOT THE ISSUE.

AS LONG AS YOU AND THE TEAM HAVE THE SENSE THAT THIS CAN BE -- THERE'S PLASTICITY HERE, RIGHT, IN TERMS OF HOW THE BOARD FEELS ABOUT THE BEST APPROACH. I THINK THE LETTER, THE LOI. THE LOI IS A VERY IMPORTANT STEP. I AGREE WITH YOU. IT WILL SAVE PEOPLE TIME. SO I'M FINE WITH THAT. AND, AGAIN, I REALLY LIKE THE FUNDING MECHANISM, WHICH IS

WHAT WE'RE REALLY FOCUSING ON HERE TO RECOMMEND TO THE FULL BOARD, THAT THESE FUNDING MECHANISMS ARE GREAT AND WILL MATTER A LOT. SO I'LL STOP THERE.

MR. TOCHER: THANK YOU, PAT. LEONDRA, I THINK I SAW YOUR HAND COME UP A COUPLE TIMES.

DR. CLARK-HARVEY: IT DID. I WANT TO JUST -- AND I SEE, MARK, YOU PUT UP YOUR HAND AS WELL. BUT I JUST WANT TO PULL OUT THAT IN SOME OF OUR MORE DRILL-DOWN GROUPS, WE DID TALK ABOUT SOME OF THE GAPS AND DEFICITS ACROSS NEURO AND WHAT'S PASSING AROUND THE DIVERSITY THERE.

AND SO I WOULD HOPE THAT WHATEVER APPROACH WE MOVE FORWARD WITH, THAT WE'RE REALLY PAYING ATTENTION TO THE FEEDBACK THAT CAME BACK OUT OF THOSE MEETINGS BECAUSE WE DID GET REALLY -- I'M SORRY. I CAN'T REMEMBER THE EXACT DATES -- BUT THIS PAST YEAR I REMEMBER SOME MEETINGS WHERE WE GOT REALLY DEEP INTO SOME OF THE DEFICITS, SOME OF THE GAPS, SOME OF THE AREAS THAT ARE LESS LIKELY TO BE ATTENUATED JUST BECAUSE OF THE LACK OF RESEARCH IN THAT AREA. AND I DO THINK THOSE ARE OPPORTUNITIES. AND SO I'M SURE THAT THE STAFF AND THE TEAM IS WORKING ON THAT. AND I THINK THAT YOU SHOULD ALREADY HAVE A SMALL COMPENDIUM OF SOME OF OUR ON RECOMMENDATIONS AND SOME OF THE AREAS IDENTIFIED,

AND I DO HOPE THAT WE CAN KEEP THAT IN MIND.

ALSO WANT TO MENTION I THINK IT'S DIFFICULTY WITH NEURO, RIGHT. AND SO WHEN YOU'RE TALKING ABOUT WITH THE GASTROINTESTINAL, ALL OF THESE THINGS, IT SEEMS LIKE, OKAY, THAT'S A CATEGORY TO THE SIDE. WE CAN PERHAPS DO WITHOUT THAT OR NOT FOCUS THERE, BUT WE HAVE TO REMEMBER THAT ALL OF THESE THINGS CUT ACROSS WHEN YOU'RE TALKING ABOUT NEURO AND BEHAVORIAL HEALTH DISORDERS, THAT ALL OF THESE THINGS SHOW UP IN DIFFERENT WAYS FOR FOLKS THAT HAVE SPECIFIC CONDITIONS. LIKE, I REMEMBER THERE WAS A CONVERSATION WE BROUGHT IN SOME FOLKS AROUND AUTISM AND SOME WAYS THAT THINGS WERE EMERGING SPECIFICALLY FOR THOSE CLIENTS.

BOTH/AND, RIGHT? YES, LET'S FIGURE IT OUT AND CATEGORIZE AND KIND OF LINE UP IN RANK ORDER AND ALSO REMEMBER THAT THINGS AREN'T SO SEPARATE AND DISTINCT, BUT THERE'S SO MUCH INTERSECTION. SO WITH ALL THAT SAID, I WOULD ARGUE FOR MORE CONNECTION, CHECKUP WITH THE COMMITTEE ON SOME OF THE THINGS THAT WE HAVE HIGHLIGHTED. I HOPE THAT MAKES SENSE.

DR. CANET-AVILES: GOOD POINT. THANK YOU, LEONDRA.

MR. TOCHER: MARK, YOUR HAND IS RAISED.

CHAIRMAN FISCHER-COLBRIE: YEAH. GOOD

COMMENTS THERE. AND I THINK IT'S GOING TO BE INCUMBENT TO ENSURE THAT WE HAVE A PLACEHOLDER HERE FOR A COMMENT, IF YOU WILL, IN THE CONTEXT THAT A NUMBER OF THINGS ARE GOING TO COME TO THE HEAD ON THE PRESUBMISSION DIALOGUE. AND EVEN AHEAD OF THAT, TO PAT'S POINT, EVEN THE COMMUNICATION AROUND PRESUBMISSION WORK WILL REQUIRE CAREFUL THOUGHT ABOUT THE LANGUAGE BEING SENT OUT TO PEOPLE AROUND THAT. SO THAT'S GOING TO TAKE SOME WORK, POSSIBLY SOME TESTING, IF YOU WILL, WITH RESEARCHERS TO ENSURE THAT WE'VE GOT THE PROPER COMMUNICATION GOING ON WITH THEM TO ENSURE THAT SOME GRANTEE THAT MIGHT HAVE -- DOESN'T GET CHOPPED OFF BECAUSE THEY THINK THE PROCESS IS GOING TO BE PROBLEMATIC TYPE OF THING. SO I JUST WANTED TO MAKE THAT NOTATION AND CALL THAT OUT SPECIFICALLY, TIE BACK TO LEONDRA'S AND TO PAT'S COMMENTS.

DR. LEK TAN: THANK YOU, MARK. I THINK THAT'S SOMETHING THAT WAS EXTREMELY IMPORTANT. WE REALIZE THE IMPORTANCE OF THAT MESSAGING TO THE APPLICANTS AS WELL. WE'VE PUT A LOT OF THOUGHT INTO IT AND WILL BRING YOU OUR DECISION AND DESIGN AT THE APPROPRIATE TIME WITH GIL. THANK YOU.

MR. TOCHER: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: I JUST WANTED TO

133 HENNA COURT, SANDPOINT, IDAHO 83864
208-255-5453 208-920-3543 DRAIBE@HOTMAIL.COM

REEMPHASIZE THAT WHAT WE ANTICIPATE WILL COME TO THE BOARD IN MARCH, WHICH IS GIL PROVIDING A LOT OF THE DETAIL AROUND HOW ALL OF THIS GETS ADJUDICATED INTERNALLY, EXTERNALLY, WHO'S RESPONSIBLE FOR WHAT, AT WHAT POINT THE GWG TAKES OVER, WHAT THE BOARD IS NO LONGER SORT OF RESPONSIBLE FOR, AND IT GOES INTERNAL. AND I THINK THAT THAT'S REALLY WHAT'S MISSING IN ORDER TO COMPLETELY FEEL LIKE ALL THE BASES ARE COVERED. AND SO I THINK THAT'S JUST SOMETHING REALLY IMPORTANT FOR US TO LOOK FORWARD TO IN MARCH. THANKS, GIL.

DR. CANET-AVILES: HE GAVE A THUMBS UP.

MR. TOCHER: MARK, I DON'T SEE ANY OTHER HANDS RAISED FROM THE BOARD.

CHAIRMAN FISCHER-COLBRIE: OKAY. ANY OTHER QUESTIONS FROM THE PUBLIC OR COMMENTS?

MR. TOCHER: LOOKS LIKE THERE ARE NOT, MARK.

CHAIRMAN FISCHER-COLBRIE: OKAY. WELL, LET'S PROCEED TO A ROLL CALL VOTE.

MR. TOCHER: GREAT. AND THE MOTION IS TO RECOMMEND TO THE ICOC APPROVAL OF THE DISC4 CONCEPT.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

MR. TOCHER: LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: YES.
MR. TOCHER: DEBORAH DEAS.
DR. DEAS: YES.
MR. TOCHER: MARK FISCHER-COLBRIE.
CHAIRMAN FISCHER-COLBRIE: YES.
MR. TOCHER: ELENA FLOWERS.
DR. FLOWERS: YES.
MR. TOCHER: JUDY GASSON.
DR. GASSON: YES.
MR. TOCHER: JEFF GOLDEN.
DR. GOLDEN: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: YES.
MR. TOCHER: PAT LEVITT.
DR. LEVITT: YES.
MR. TOCHER: CAROLYN MELTZER.
DR. MELTZER: YES.
MR. TOCHER: CHRIS MIASKOWSKI.
DR. MIASKOWSKI: YES.
MR. TOCHER: MARV SOUTHARD. SORRY, MARV. ARE YOU STILL ON THE CALL?
DR. SOUTHARD: YES.
MR. TOCHER: OKAY. THANK YOU. CAME IN

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LOUD AND CLEAR.

KAROL WATSON.

DR. WATSON: YES.

MR. TOCHER: KEITH YAMAMOTO.

DR. YAMAMOTO: YES.

MR. TOCHER: GREAT. THANK YOU, KEITH. THE MOTION CARRIES UNANIMOUSLY. MARK.

CHAIRMAN FISCHER-COLBRIE: GREAT. WE GOT THROUGH THOSE TWO APPROVALS. LET'S MOVE ON TO THE NEXT TOPIC FOR DISCUSSION, WHICH I THINK IS THE PRECLINICAL DEVELOPMENT.

DR. CANET-AVILES: SHYAM IS READY.

DR. PATEL: GOOD AFTERNOON. MY NAME IS SHYAM PATEL. AND ON BEHALF OF THE PRECLINICAL DEVELOPMENT TEAM, I THANK THE MEMBERS OF THE SCIENCE SUBCOMMITTEE AND THE NEURO TASK FORCE FOR THE OPPORTUNITY TO PRESENT THE PDEV CONCEPT TO YOU.

SO AS DR. CLARK-HARVEY NOTED, THE PDEV CONCEPT IS PRECLINICAL DEVELOPMENT. AND I'LL DESCRIBE HOW THAT CONCEPT IS BEING DEVELOPED AND HOW IT COMBINES AND CONSOLIDATES SOME OF OUR EXISTING PROGRAMS AND ADDS SOME NEW FEATURES AS WE GO FORWARD.

QUICK NOTE, I UNFORTUNATELY HAVE A HARD TIME PRONOUNCING THE WORD "PRECLINICAL" AND

"REGENERATIVE", SO I'M GOING TO TRY TO AVOID USING BOTH OF THOSE WORDS AS MUCH AS POSSIBLE IN THIS PRESENTATION.

SO THE OUTLINE FOR THIS PRESENTATION IS VERY SIMILAR TO THE OTHER ONE THAT YOU'VE HEARD SO FAR. I'M GOING TO SPEND A LITTLE BIT MORE TIME ON THE BACKGROUND AND THE STRUCTURE BECAUSE THIS IS NEW, BUT THE OTHER ELEMENTS ARE VERY CONSISTENT WITH WHAT YOU'VE HEARD SO FAR.

SO FIRST OF ALL, THIS PROGRAM IS MEANT TO RESPOND TO GOAL 4 IN THE SAF RECOMMENDATION, WHICH IS TO PROPEL 15 TO 20 THERAPIES TARGETING DISEASES AFFECTING CALIFORNIANS TO LATE STAGE TRIALS. AND THE RECOMMENDATION THAT WAS APPROVED BY THE BOARD AT THAT TIME INCLUDED TWO IMPORTANT POINTS. THE FIRST WAS TO CONSOLIDATE OUR EXISTING PRECLINICAL DEVELOPMENT PROGRAMS, ACCELERATE THAT DEVELOPMENT AND THAT PROGRESSION TO IND. AND THE SECOND WAS TO INCORPORATE PRIORITIZATION TO FOCUS ON INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT CALIFORNIANS.

NOW, I'LL TOUCH UPON BOTH OF THOSE POINTS THROUGHOUT THIS PRESENTATION. SO BEFORE WE GET TO THE DESIGN OF THE PROGRAM, WE WANTED TO TALK A LITTLE BIT ABOUT THE EXTERNAL LANDSCAPE AS WELL AS THE INTERNAL LANDSCAPE THAT INFORMED THE DESIGN OF

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THIS PROGRAM.

SO THIS SLIDE IS MEANT TO CONVEY A SINGULAR POINT, WHICH IS THAT OVER THE LAST DECADE THERE HAS BEEN A HUGE GROWTH BOTH ON THE COMMERCIAL SIDE AS WELL AS ON THE PRECOMMERCIAL SIDE OF CELL AND GENE THERAPY CANDIDATES.

AND WHAT THIS SLIDE DEMONSTRATES IS THE VAST NUMBER OF PRECLINICAL AND CLINICAL STAGE CELL AND GENE THERAPY CANDIDATES IN DEVELOPMENT. WHAT'S WORTH NOTING HERE IS THAT EVEN DESPITE THE SIGNIFICANT OVERREPRESENTATION OF SOLID AND BLOOD CANCERS, BOTH CELL AND GENE THERAPIES HAVE BEEN TARGETED AT MULTIPLE THERAPEUTIC AREAS, ALL MAJOR THERAPEUTIC AREAS REPRESENTED HERE. AND THIS HIGHLIGHTS THE FACT THAT THERE'S WAY MORE DEMAND FOR FUNDING THAN CIRM CAN POTENTIALLY PROVIDE FOR CELL AND GENE THERAPIES.

DESPITE THIS SIGNIFICANT GROWTH IN THE FIELD, THERE IS, HOWEVER, A CHALLENGE ON THE INVESTMENT SIDE. SO OVER THE PAST FEW YEARS, VENTURE INVESTMENT IN CELL AND GENE THERAPIES ACTUALLY FLATLINED COMPARED TO BIOLOGICS AND SMALL MOLECULES. AND THE BAR FOR INVESTMENT IN CELL AND GENE THERAPY DEVELOPMENT HAS GOTTEN PROGRESSIVELY HIGHER OVER THE YEARS. AT THIS POINT MOST OF THE

VENTURE INVESTMENT AND BIOPHARMA PARTNERSHIP DOLLARS ARE FOCUSED ON CLINICAL STAGE COMPANIES AND CLINICAL STAGE CANDIDATES. IN FACT, WE SEE THIS IS OUR OWN PORTFOLIO WHERE, DESPITE OVER $2 BILLION OF INDUSTRY SUPPORT FLOWING INTO CIRM-FUNDED PROGRAMS LAST YEAR IN 2024, ONLY A SMALL FRACTION OF THAT WAS ACTUALLY DEDICATED TO PRECLINICAL STAGE COMPANIES.

SO WITH THAT LEARNING IN PLACE, WHAT THAT HIGHLIGHTS IS THAT THERE IS STILL A VERY CRITICAL NEED FOR CIRM ACCELERATE CELL AND GENE THERAPY DEVELOPMENT THROUGH THE PROTOTYPICAL TRANSLATIONAL VALLEY OF DEATH TO FIRST-IN-HUMAN CLINICAL TRIALS. AND ON THIS SLIDE I'M GOING TO HIGHLIGHT SOME OF THE OBSERVATIONS WE'VE BEEN MAKING OVER THE LAST DECADE OF RUNNING THESE PROGRAMS.

AND SO CIRM'S FUNDING PROGRAMS OVER THE LAST DECADE HAVE HAD PROGRESSIVE, BUT DISTINCT FUNDING OPPORTUNITIES FOR PRECLINICAL DEVELOPMENT. SO, FIRST OF ALL, THERE'S CANDIDATE DISCOVERY, WHICH IS THE DISC2 PROGRAM HERE IN YELLOW. UPON DECLARING A SINGULAR CANDIDATE, THE AWARDEE WOULD APPLY FOR A TRAN1 AWARD WHERE THAT WOULD SUPPORT ALL THE PRECLINICAL DEVELOPMENT ACTIVITIES LEADING UP TO AND COMPLETION OF AN FDA PRE-IND MEETING. UPON ACHIEVING THAT OUTCOME, THE AWARDEE WOULD APPLY TO A

CLIN1 PROGRAM. HERE THE CLIN1 AWARD WOULD SUPPORT THEM ALL THE WAY TO IND FILING. SO THREE DISTINCT FUNDING OPPORTUNITIES MEANT TO BE PROGRESSIVE, MEANT TO SUPPORT PROJECTS AT THE STAGE THEY'RE AT, BUT BEING DISTINCT IN THAT NATURE.

AND SO WHAT I'M GOING TO HIGHLIGHT IN THE IT NEXT FEW BUBBLES ARE ACCELERATION OBSERVATIONS WE'VE BEEN MAKING AS WELL AS SCOPE OBSERVATIONS THAT WE HOPE TO ADDRESS IN THE NEW PDEV PROGRAM.

SO FIRST AND FOREMOST, MULTIPLE TRAN1 AWARDS HAVE ACTUALLY PROGRESSED TO PRE-IND MEETING EARLIER THAN EXPECTED. THIS CAN BE A FEW MONTHS OR IT COULD BE A COUPLE YEARS EARLIER THAN EXPECTED. THIS REQUIRES AWARD AMENDMENTS TO USE THE REMAINING FUNDING TO CONDUCT STUDIES INFORMED BY FDA FEEDBACK. NOW, THIS IS A SIGN OF A MATURING FIELD, AND WE EXPECT THIS TREND TO CONTINUE GOING FORWARD. HOWEVER, AFTER CONDUCTING THAT PRE-IND MEETING, THERE'S ONLY A LIMITED NUMBER OF ACTIVITIES THAT ARE ACTUALLY ALLOWED IN THE TRAN1 AWARD BASED ON THE PROGRAM.

AND SO AWARDEES THAT HAVE CONDUCTED THEIR PRE-IND MEETING AND HAVE SUCCESSFULLY SECURED CLIN1 FUNDING ARE OFTEN HAVING A SIGNIFICANT LAG TIME FROM HAVING THAT PRE-IND MEETING TO THE CLIN1 AWARD

START. THE MEDIAN TIME THERE IS 16 MONTHS.

ON THE SIDE OF SCOPE, ONE OF THE THINGS I WANT TO HIGHLIGHT IS THAT THERE COULD BE SEVERAL TRAN STAGE PROJECTS THAT MIGHT WANT TO CONDUCT SOME FOCUSED OPTIMIZATION OF THEIR PROJECT. THIS IS PARTICULARLY RELEVANT IN GENE THERAPIES WHERE THEY MAY WANT TO OPTIMIZE THE RNA SEQUENCE, FOR EXAMPLE, OR CHANGE OUT A PROMOTER. IN THIS PARTICULAR INSTANCE, WITH THAT TYPE OF OPTIMIZATION IN OUR CURRENT PROGRAMS, THEY'D ACTUALLY HAVE TO APPLY FIRST TO A DISC2 AWARD, CONDUCT THAT OPTIMIZATION, AND THEN APPLY TO TRAN1.

SIMILARLY, APPLICATIONS THAT ARE WITHIN SIX TO TWELVE MONTHS OF A PRE-IND MEETING DON'T REALLY FIT INTO THE TRAN1 OR CLIN1 FUNDING MECHANISM BECAUSE THE OUTCOME OF TRAN1 IS A PRE-IND MEETING, AND THE REQUIREMENT FOR CLIN1 IS TO ACTUALLY HAVE CONDUCTED THAT MEETING FIRST BEFORE YOU APPLY. AND SO THERE ARE THESE SCOPE CHALLENGES AS WELL AS ACCELERATION OPPORTUNITIES.

SO PUTTING ALL THIS INTO CONTEXT, WE THINK THAT THERE'S A CLEAR OPPORTUNITY FOR CIRM TO EVOLVE ITS FUNDING PROGRAM TO BETTER ADDRESS THESE TYPES OF OPPORTUNITIES AND CHALLENGES AND HAVE A HOLISTIC FOCUS ON GETTING THESE PROGRAMS TO FIRST-IN-HUMAN

CLINICAL TRIALS.

IN FACT, OTHER FUNDING AGENCIES, PARTICULARLY NIH, HAS DEVELOPED OVER THE LAST FEW YEARS INNOVATIVE FUNDING PROGRAMS THAT ARE MORE HOLISTIC IN NATURE FOR CELL AND GENE THERAPY DEVELOPMENT. SO THESE PROGRAMS HAVE TWO THINGS IN COMMON. FIRST IS THAT THEY ALLOW FOR MULTIPLE ENTRY POINTS. SO THE PROJECT CAN APPLY AND ENTER AT THE STAGE THAT IT'S AT IN THE PRECLINICAL DEVELOPMENT STAGE. AND SECONDLY, IT WILL SUPPORT PROJECTS ACROSS MULTIPLE CLASSICAL STAGES OF PRODUCT DEVELOPMENT. SO EVERYTHING FROM LEAD OPTIMIZATION TO IND FILING. SOME OF THESE PROGRAMS EVEN THROW IN CLINICAL TRIAL SUPPORT AS PART OF THAT PROJECT.

SO PUTTING ALL THOSE LEARNINGS TOGETHER AND LOOKING AT THE LANDSCAPE EXTERNALLY, INTERNAL LANDSCAPE, AND LEARNINGS FROM OTHER FUNDING OPPORTUNITIES, AS WELL AS OUR OWN, WE'RE PROPOSING THE PDEV PROGRAM WITH A SINGULAR OBJECTIVE OF ACCELERATING COMPLETION OF PRECLINICAL DEVELOPMENT, FDA IND CLEARANCE, AND CLINICAL TRIAL START-UP FOR STEM CELL-BASED AND GENETIC THERAPIES. AND SO THE OVERALL INTENT OF THIS PROGRAM IS TO HAVE A SHARED GOAL BETWEEN THE AWARDEE AND CIRM TO GET TO THAT FIRST-IN-HUMAN CLINICAL TRIAL FOR THAT PARTICULAR

THERAPY IN THAT PARTICULAR INDICATION.

EFFECTIVELY WHAT THAT MEANS IS THAT WE'RE COMBINING THE TRANSLATIONAL AND CLINICAL ONE FUNDING OPPORTUNITIES INTO A SINGULAR PROGRAM. THIS ALLOWS FOR MULTIPLE POINTS OF ENTRY. AND WE WILL FUND THOSE PROJECTS TO FIRST-IN-HUMAN CLINICAL TRIALS.

AND THIS PROGRAM, THE PDEV PROGRAM, IS MEANT TO FIT INTO THE ENHANCED STRUCTURE OF CIRM FUNDING PROGRAMS SORT OF BRACKETED BY THE EARLY DEVELOPMENT PROGRAM, EDEV, WHICH WILL BE A REPLACEMENT FOR CANDIDATE DISCOVERY PROGRAMS. THIS IS GOING TO COME TO YOU AS A PROPOSAL DOWN THE ROAD. AND IT FEEDS INTO THE CLIN2 PROGRAM, WHICH IS OUR CLINICAL TRIAL PROGRAM, WHICH IS BEING PROPOSED FOR ENHANCEMENTS THAT DR. KADYK WILL TALK ABOUT NEXT.

SO I'M GOING SPEND THE NEXT FEW SLIDES TALKING ABOUT THE CONSOLIDATION STRUCTURE OF THIS NEW PROGRAM, AND THEN WE'LL GET INTO THE PRIORITIZATION ELEMENTS.

SO AS I MENTIONED, THIS PROGRAM COMBINES EARLY TRANSLATIONAL DEVELOPMENT AS WELL AS LATE STAGE IND-ENABLING TRANSLATIONAL DEVELOPMENT. SO, AGAIN, THE PROGRAM IS DESIGNED TO SUPPORT CRITICAL PATH ACTIVITIES FROM CANDIDATE OPTIMIZATION TO TRIAL START-UP. THE PROGRAM COMES IN AT THE STAGE THAT

IT'S AT, AND WE WILL FUND IT TO IND CLEARANCE AND FIRST-IN-HUMAN CLINICAL TRIAL.

SO WHEN WE THINK ABOUT PRECLINICAL DEVELOPMENT, IT'S GENERALLY BUCKETED INTO FOUR CATEGORIES. THERE'S MANUFACTURING, NONCLINICAL TESTING, CLINICAL PLAN DEVELOPMENT, AS WELL AS REGULATORY INTERACTIONS. AND THESE TWO STAGES, YOU RECALL SORT OF TRAN-LIKE STAGE AND THE LATE CLIN1 LATE STAGE ARE INTRICATELY LINKED. SO DURING THAT YOU RECALL PRECLINICAL DEVELOPMENT STAGE, THE PROJECT IS FOCUSED ON OPTIMIZING ITS MANUFACTURING AND ANALYTICAL TECHNIQUES. IT'S DOING PILOT STUDIES ON NONCLINICAL TESTING, AND IT'S DEVELOPING ITS CLINICAL PLAN. ALL THAT IS THEN INFORMED BY A PRE-IND MEETING TO HAVE A VERY CLEAR, DEFINED PATH FOR CONDUCTING IND-ENABLING STUDIES, FOR GMP MANUFACTURING OF THE DRUG PRODUCT, AND FINALIZING THE CLINICAL PROTOCOL ALL IN SUPPORT OF FILING THAT IND APPLICATION AND GETTING CLEARANCE TO CONDUCT THE FIRST-IN-HUMAN CLINICAL TRIAL.

SO BY HAVING THIS TYPE OF A FUNDING STRUCTURE HERE, WE ALLOW THE AWARDEE TO APPROPRIATELY AND RATIONALLY DESIGN AND STAGE THESE ACTIVITIES FOR THAT PARTICULAR CANDIDATE TO OPTIMIZE THEM TO GET TO FIRST-IN-HUMAN CLINICAL TRIALS AS

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QUICKLY AS POSSIBLE.

ON THIS SLIDE I'M GOING TO DESCRIBE THE AWARD STRUCTURE. SO IN THE INTEREST OF ACCELERATION, WE'RE PROPOSING TO HAVE DISTINCT FUNDING CAPS AND DURATION LIMITS FOR EACH OF THESE TWO STAGES. SO AS A REMINDER, THE PROGRAM CAN COME IN AT THE STAGE IT'S AT; BUT IF IT'S REQUESTING FUNDING FOR EARLY PDEV STAGE, IT'S GOING TO HAVE A MAXIMUM AMOUNT OF $5.5 MILLION TOTAL COST THEY CAN REQUEST. AND THE MAXIMUM STAGE DURATION IS 30 MONTHS.

IF IT'S REQUESTING FUNDING FOR LATE STAGE IND-ENABLING, WHICH ALL OF THEM SHOULD BE, THE MAXIMUM STAGE AMOUNT WOULD BE $7.5 MILLION TOTAL COST, AND THE MAXIMUM STAGE DURATION IS 30 MONTHS.

SO AS A RECAP, WE CAN HAVE PROJECTS THAT ARE REQUESTING FUNDING FOR BOTH THE EARLY PDEV AND LATE PDEV STAGES OR JUST THE LATE PDEV STAGE DEPENDING ON WHERE IT'S AT ALONG THAT SPECTRUM OF PRECLINICAL DEVELOPMENT. SO PUTTING ALL THAT TOGETHER, THE MAX AWARD AMOUNT THAT CIRM CAN GIVE OUT WOULD BE $13 MILLION, AND THE MAX AWARD DURATION UNDER THIS PROGRAM WOULD BE FIVE YEARS.

SO I'M GOING TO TAKE A MINUTE TO TALK ABOUT THE PRIORITIZATION, AND THEN WE'LL COME BACK

AROUND AGAIN TO THE STRUCTURE OF THIS PROGRAM. SO AGAIN, AS A REMINDER, THE SAF RECOMMENDATION IS TO INCORPORATE PRIORITIZATION OF INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT CALIFORNIANS. AND OUR INTENT HERE IS SIMILAR TO WHAT YOU'VE HEARD IN THE PREVIOUS TWO INSTANCES, IS TO INCORPORATE A PREFERENCE-BASED MECHANISM THAT ALLOWS US TO FOCUS THE FUNDING TO THE MOST RESPONSIVE PROJECTS THAT CIRM RECEIVES.

SO I'M GOING TO FIRST DESCRIBE THE SORT OF GUIDING PRINCIPLES FOR THE PRIORITIZATION AND THE IMPLEMENTATION PLAN. SO THE GUIDING PRINCIPLES HERE ARE FOCUSED ON FUNDING THERAPIES THAT OFFER POTENTIAL FOR TRANSFORMATIVE CLINICAL IMPACTS, BUT THAT ALSO ADDRESS BOTTLENECKS TO PATIENT ACCESS AND AFFORDABILITY. WE'RE ALL VERY AWARE OF EXISTING BOTTLENECKS IN THE CELL AND GENE THERAPY DELIVERY SYSTEM FOR PATIENTS WITH RESPECT TO ACCESS AND AFFORDABILITY. AND WE WANT THESE PROGRAMS AND NEXT GENERATION TO ADDRESS SOME OF THOSE CHALLENGES.

AND LASTLY, TO FUND THERAPIES THAT ARE NOT ADEQUATELY SUPPORTED BY FEDERAL FUNDING OR PRIVATE INVESTMENT.

AND THIS IS RELEVANT BECAUSE I MENTIONED SEVERAL EXISTING NIH OR OTHER FUNDING AGENCIES'

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PROGRAMS. AND WHAT I DID NOT MENTION AT THAT TIME WAS THAT THOSE VARIOUS PROGRAMS HAVE A LIMITATION THAT CIRM'S FUNDING MODEL OVERCOMES, WHICH IS THAT THEY HAVE LIMITED PROGRAM BUDGETS, LIMITED AWARD AMOUNTS, AND INFREQUENT FUNDING CYCLES.

SO THE IMPLEMENTATION PLAN FOR THE PREFERENCES IS SIMILAR TO WHAT DR. LEK TAN DESCRIBED PREVIOUSLY FOR DISC4. HERE THE GOAL IS TO BUILD A DIVERSE PORTFOLIO OF THERAPEUTIC APPROACHES AND TO ADAPT AND EVOLVE THE PREFERENCES ON AN ANNUALIZED BASIS TO HELP CONSTRUCT THAT DIVERSE PORTFOLIO.

SO THE PRIORITIES THAT WE'LL PRESENT TO THE BOARD ARE INFORMED BY INTERNAL PORTFOLIO AND EXTERNAL LANDSCAPE ANALYSES. AND THE INTENT HERE IS TO PRESENT THIS INFORMATION AND PROPOSE PREFERENCES TO THE BOARD ON AN APPROXIMATE FISCAL YEAR BASIS TO HELP CONSTRUCT THAT DIVERSE PORTFOLIO AND TO ACCOUNT FOR CHANGES THAT ARE HAPPENING IN THE FIELD.

SO WITH THAT IN MIND, FOR THIS FIRST FISCAL YEAR FOR THE PDEV PROGRAM, WE ARE PROPOSING A SET OF PREFERENCES THAT ARE EITHER, ONE, RESPONSIVE TO PROP 14 PRIORITIES OR RESPONSIVE TO THE ACCELERATION FOCUS OF THE PROGRAM. AND SO I'M GOING TO WALK THROUGH A FEW OF THESE.

THE FIRST THREE PRIORITIES HERE, THE FIRST

THREE PREFERENCES HERE ARE FOCUSED ON MODALITIES THAT CAN POTENTIALLY ADDRESS PATIENT ACCESS AND AFFORDABILITY BARRIERS. SO THIS INCLUDES PLURIPOTENT STEM CELL-DERIVED THERAPIES WHICH COULD REPRESENT AN ABUNDANT RENEWABLE SOURCE FOR CELL THERAPIES, IN VIVO GENETIC THERAPIES, WHICH COULD OVERCOME SOME OF THE LIMITATIONS, EX VIVO GENETIC THERAPIES BY ADDRESSING THOSE PATIENT ACCESS AND AFFORDABILITY BARRIERS, AND LASTLY NONVIRAL NUCLEIC ACID DELIVERY MECHANISMS WHICH CAN OVERCOME THE EXISTING LIMITATIONS OF BIOMETRIC DELIVERY SYSTEMS.

THE FOURTH PREFERENCE, ALSO IN RESPONSE TO PROP 14 PRIORITY, IS FOR DISEASES OF THE BRAIN AND CNS. THE LAST TWO PREFERENCES THAT I MENTIONED ARE RESPONSIVE TO THE ACCELERATION FOCUS. SO THE PREFERENCE FOR DISC2 AND TRAN1 AWARDS ARE PROGRESSING FROM OUR PORTFOLIO. AND LASTLY, A PREFERENCE FOR PROGRAMS THAT ARE INFORMED BY FDA INTERACTIONS WHETHER THEY BE INTERACT MEETING OR A PRE-IND MEETING.

THESE PREFERENCES WILL BE FACTORED IN DURING THE PRESUBMISSION PROCESS VERY SIMILAR TO WHAT DISC4 HAS IN MIND. AND THEY COULD ALSO BE FACTORED IN DURING THE ARS REVIEW BY THE BOARD.

SO I'M GOING TO GO THROUGH THE NEXT FEW

SLIDES WALKING THROUGH SOME OF THE STANDARD FEATURES OF THAT PROGRAM AS WELL AS SOME OF THE NEW FEATURES. SO ON THIS SLIDE I'M GOING TO POINT OUT A COUPLE OF THINGS. SO FIRST OF ALL, THE PDEV PROGRAM WILL BE OFFERED TWICE A YEAR. IT WILL BE LIMITED TO CALIFORNIA APPLICANTS ONLY. SO NON-PROFIT OR FOR-PROFIT APPLICANTS THAT ARE BASED IN CALIFORNIA AND MEET THE DEFINITION OF A CALIFORNIA ORGANIZATION. THERE WILL BE A CO-FUNDING REQUIREMENT FOR FOR-PROFITS AND PARTNERED NON-PROFITS. THIS IS IDENTICAL TO THE EXISTING TRAN1 AND CLIN1 CO-FUNDING REQUIREMENTS.

WE HAVE GRANTS OF ESTIMATED PROJECTIONS TO ESTIMATE A PIPELINE THAT WOULD RESPOND TO THE SAF GOAL 4. AND BASED ON THAT, FOR THE FIRST FISCAL YEAR, WE'RE REQUESTING THE PROGRAM BUDGET OF $160 MILLION. DEPENDING ON THE NATURE OF THE AWARDS THAT COME IN, WHETHER THEY'RE ASKING FOR BOTH STAGES OF DEVELOPMENT OR JUST THE LATE STAGE, THE NUMBER OF AWARDS THAT CAN BE FUNDED ARE 12 TO 21 PER YEAR WITH THAT FISCAL YEAR BUDGET. HERE IN THIS TABLE WE'RE DISPLAYING A PROJECTION AS A REPRESENTATIVE EXAMPLE WHERE THIS AMOUNT OF FUNDING COULD POTENTIALLY FUND SEVEN EARLY PDEV AWARDS AND NINE LATE PDEV AWARDS. AND THIS WOULD STRIKE A BALANCE BETWEEN SUPPORTING

INNOVATIVE, EARLY STAGE THERAPIES AS WELL AS ACCELERATING PROJECTS TO CLINICAL PIPELINE BY SUPPORTING THOSE LATE STAGE PDEV AWARDS.

AS YOU'RE AWARE, EVERY APPLICANT HAS TO MEET CERTAIN ELIGIBILITY REQUIREMENTS. FOR THE PDEV PROGRAM, THESE ELIGIBILITY REQUIREMENTS ARE LARGELY SIMILAR TO THE EXISTING TRAN1 AND CLIN1 PROGRAM REQUIREMENTS. SO, FOR EXAMPLE, THIS INCLUDES CANDIDATE READINESS REQUIREMENTS, PI AND PROJECT MANAGER MINIMUM EFFORT REQUIREMENTS, THE ABILITY TO DEMONSTRATE THE CO-FUNDING AT THE TIME OF APPLICATION, AND TO DEMONSTRATE THE ABILITY TO REACH THE EXPECTED OUTCOME, WHICH IS IND SUBMISSION AND CLEARANCE.

SO ON THE NEXT COUPLE SLIDES, I'LL DEFINE SOME OF THE NEW FEATURES, MODIFIED FEATURES OF THIS PROGRAM COMPARED TO OUR EXISTING PROGRAMS. SO AS DR. LEK TAN MENTIONED, THIS PROGRAM WILL INCORPORATE A PRESUBMISSION PROCESS. THIS IS MEANT TO MANAGE THE HIGH APPLICATION VOLUMES. IT'S ALSO MEANT TO REDUCE THE BURDEN FOR APPLICANTS BECAUSE THEY'RE SUBMITTING A PRESUBMISSION ON WHICH CIRM IS IMPLEMENTING ITS PROGRAM PREFERENCES. AND THIS ALSO ALLOWS CIRM TO PREPLAN THE GRANTS WORKING GROUP COMPOSITION AND HAVE A MORE ROBUST SCIENTIFIC REVIEW

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WHEN THOSE APPLICATIONS COME IN AND ARE REVIEWED BY THE GWG.

SPEAKING OF THE GWG REVIEW, THIS PROGRAM WILL ADOPT THE 1 TO 100 NUMERICAL SCORING SYSTEM FOR GWG. AND THIS WILL ALIGN ACROSS ALL CIRM PROGRAMS. AND THAT'S SORT OF A RANGE OF SCORING IMPROVES GRANULARITY AND VISIBILITY FOR SCORE-DRIVING DECISIONS.

SO THIS SLIDE WILL HIGHLIGHT SOME OF THE REQUIREMENTS THAT ARE MEANT TO BROADLY SUPPORT AND REDUCE BOTTLENECKS TO DEVELOPMENT OF CELL AND GENE THERAPIES AS WELL AS TO AIM FOR PLANNING FOR COMMERCIALIZATION. SO FIRST AND FOREMOST, AS YOU ALL KNOW, CELL AND GENE THERAPIES DEVELOPMENT NEEDS TO FOCUS VERY EARLY ON ON ACCESS AND AFFORDABILITY MARKET ACCESS. AND SO WE'LL BE REQUIRING STAGE APPROPRIATE MARKET ACCESS PLANNING ACTIVITIES ACROSS BOTH THE PDEV AND CLIN2 PROGRAMS WITH A PARTICULAR FOCUS ON ACCESS AND AFFORDABILITY PLANNING. AND WE'RE CURRENTLY WORKING WITH CONSULTANTS TO DEVELOP A ROADMAP OF WHAT ARE STAGE APPROPRIATE ACTIVITIES ACROSS PRECLINICAL AND CLINICAL DEVELOPMENT, AND THEN TO INCORPORATE THAT ROADMAP INTO THE EVALUATION OF APPLICATIONS AS WELL AS SUPPORT FOR CONDUCTING THOSE ACTIVITIES OVER THE COURSE OF A PDEV AWARD.

THIS PROGRAM WILL ALSO INCORPORATE THE DATA SHARING AND MANAGEMENT PLAN REQUIREMENTS IN COORDINATION WITH CIRM'S OVERARCHING DATA INITIATIVES. AND THE LAST POINT HERE IS A TOP PRIORITY FOR THE PDEV TEAM. WE WANT TO BE ABLE TO REQUIRE AND FACILITATE PRECOMPETITIVE SHARING BETWEEN OUR PDEV AWARDEES, EFFECTIVELY CREATING A KNOWLEDGE NETWORK OF OUR PDEV AWARDEES WHERE THEY CAN SHARE BEST PRACTICES FOR REGULATORY INTERACTIONS, FOR STUDY DESIGNS, FOR ASSAY DEVELOPMENT ALL WITH THE AIM OF HELPING ALL THE PROGRAMS ADVANCE TO FIRST-IN-HUMAN CLINICAL TRIALS.

AND IN THE SPIRIT OF ADVANCING ALL PROJECTS, WE ARE ALSO MAKING SOME ENHANCEMENTS TO OUR AWARD MANAGEMENT PRACTICES. SO FIRST AND FOREMOST, WE ARE COMMITTING TO HAVING A MORE PROACTIVE AWARD MANAGEMENT APPROACH THAT INCREASES REAL-TIME INTERACTIONS BETWEEN CIRM AND THE AWARDEE PROJECT TEAMS. THIS ALSO INCORPORATES RELEVANT EXPERTISE FROM THE MANUFACTURING LEADERSHIP OF THOSE PROJECT TEAMS, AND IT ALSO ENSURES THAT CIRM IS PARTICIPATING MEANINGFULLY IN THE FDA MEETINGS.

WE ARE ALSO PROPOSING TO INCORPORATE AN EXTERNAL PRODUCT DEVELOPMENT EXPERT NETWORK OF EXTERNAL CONSULTANTS IN PRECLINICAL DEVELOPMENT, IN

CLINICAL DEVELOPMENT, REGULATORY EXPERTISE, AS WELL AS DISEASE AREA EXPERTISE THAT WILL SUPPORT CIRM SCIENCE OFFICERS AND PROJECT TEAMS TO ACCELERATE THESE PROJECTS TO IND CLEARANCE. SO THIS, IN EFFECT, IS MEANT TO COMPLEMENT THE INTERNAL EXPERTISE OF THE CIRM SCIENCE OFFICERS AND TO BE A BRAIN TRUST THAT THE SCIENCE OFFICERS AS WELL AS THE AWARDEE TEAMS CAN LEVERAGE TO HELP SUPPORT THEIR ACTIVITIES AND THEIR PLANNING AS THEY PROGRESS THROUGH THE STAGES OF PRECLINICAL DEVELOPMENT.

WE WILL ALSO RETAIN THE OPERATIONAL MILESTONE-DRIVEN AWARD MANAGEMENT STRUCTURE OF CLIN1. AND IN THIS PARTICULAR INSTANCE, AS A REMINDER, ALL OF OUR TRANSLATIONAL, CLINICAL AWARDS ARE MILESTONE DRIVEN. AND SO CIRM WILL MAKE A DISBURSEMENT THAT ALLOWS THE AWARDEE TO REACH THE PREDEFINED OPERATIONAL MILESTONE. ONCE THAT MILESTONE HAS BEEN REACHED, THE SECOND DISBURSEMENT IS MADE, ALLOWING THEM TO GET TO THAT NEXT MILESTONE. AND SO THAT'S A WAY TO EFFECTIVELY DERISK CIRM'S INVESTMENT IN THESE PROJECTS AND TO ALSO ENSURE THAT THERE'S TIMELY ACHIEVEMENT OF THOSE MILESTONES AND THAT THEY'RE OBJECTIVELY MET.

SO WE'LL ALSO LEVERAGE OUR PROACTIVE COMMUNICATION COMMITMENT TO MAKE SURE THAT WE CAN

MITIGATE ANY PROJECT DELAYS THAT MIGHT ARISE OVER THE COURSE OF THAT PROJECT.

SO I'M GOING TO END ON THIS SLIDE, WHICH IS DEMONSTRATING THE FIRST CYCLE. SO IF THE BOARD APPROVES THIS CONCEPT AT THE END OF MARCH, WE'RE EXPECTING TO ROLL OUT THE PROGRAM WITHIN THE NEXT TWO MONTHS. AND AT THE MOMENT, THE CYCLE FROM PRESUBMISSION TO AWARD CONTRACTING IS ESTIMATED TO BE ABOUT TEN MONTHS.

SO IN SUMMARY, THE OBJECTIVE OF THE PDEV PROGRAM IS TO ACCELERATE PRECLINICAL DEVELOPMENT TO FIRST-IN-HUMAN CLINICAL TRIALS OF STEM CELL-BASED AND GENETIC THERAPIES. THE EXPECTED OUTCOME IS IND CLEARANCE OF THOSE THERAPIES FOR THAT INDICATION. WE WILL SUPPORT ALL NECESSARY ACTIVITIES TO GET TO THAT OUTCOME. AND LASTLY, WE WILL TO FOCUS THE FUNDING FOR MAXIMAL IMPACT, WE WILL INCORPORATE A SET OF PREFERENCES THAT ARE REVIEWED ANNUALLY BY THE BOARD.

SO WITH THAT, WE REQUEST A MOTION FROM THE SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE TO RECOMMEND APPROVAL TO THE FULL ICOC OF THE PDEV CONCEPT. THANK YOU.

CHAIRMAN FISCHER-COLBRIE: THANK YOU SO MUCH, SHYAM. GREAT PRESENTATION. I REALLY

APPRECIATE IT WITH AN EDITORIAL COMMENT THAT THIS HAS THE OPPORTUNITY TO ACCELERATE THE PROCESS OF GETTING THINGS INTO CLINICAL TRIALS. VERY INTERESTING PROPOSAL HERE. AND WITH THAT, I'D LIKE TO CALL FOR A MOTION AND A SECOND.

DR. YAMAMOTO: SO MOVED.

DR. SOUTHARD: SOUTHARD SECONDS.

CHAIRMAN FISCHER-COLBRIE: THANK YOU. AND LET'S OPEN IT UP FOR DISCUSSION AND QUESTIONS BY THE COMMITTEES.

DR. LEVITT: I GUESS I'LL START. WHAT A REPUTATION. THIS IS LIKE KINDERGARTEN ALL OVER AGAIN FOR ME.

SO THAT WAS GREAT. I LOVE THE CONCEPT. I THINK YOU'RE RIGHT. IT'S GOING REALLY SPEED THINGS UP IN A BIG WAY.

THE SHARING COMPONENT WHICH YOU'VE SORT OF -- YOU MENTIONED, HOW DO YOU THINK THAT'S GOING TO WORK? BECAUSE LET'S SAY, I DON'T KNOW, LET'S SAY JEFF GOLDEN DISCOVERS THROUGH HIS RESEARCH THIS AMAZING ASSAY THAT COSTS $1 INSTEAD OF A $1,000 AND THEY'RE IN THE PROCESS OF USING IT FOR SOME SCREENING OF SOME SORT AND THEN PUT IT INTO A PROGRESS REPORT TO YOU ALL. IS THAT -- HOW IS THE SHARING GOING TO OCCUR? HE HASN'T FILED WITH HIS

TECH TRANSFER YET BECAUSE HE'S LAZY. SORRY, JEFF. AND SO HOW IS THE SHARING GOING TO WORK? HOW IS CIRM GOING TO ENFORCE THE SHARING? ENFORCING DATA SHARING ONCE PUBLISHED, THAT'S PRETTY STRAIGHTFORWARD. ENFORCING THE DATA MANAGEMENT, THE DATA MANAGEMENT APPROACH IS THEY HAVE TO HAVE A ROBUST PLAN, THAT'S ENFORCEABLE. BUT WHERE DO YOU SEE THIS OCCURRING? LIKE AT WHAT POINT IN THESE INVESTIGATIONS WHERE THIS IS GOING TO BE OCCURRING?

DR. PATEL: FIRST OF ALL, I APPRECIATE THAT YOU WENT FIRST, PAT. AND DR. GOLDEN IS BUSY. THIS JUST WILL TAKE AWHILE. SO WE WANT TO BE CAREFUL AROUND THE DATA SHARING. SO THERE'S TWO COMPONENTS TO THAT. THE KNOWLEDGE NETWORK PART IS MEANT TO BE MORE COLLABORATIVE IN NATURE. FOR EXAMPLE, THERE COULD BE SOME ASSAYS THAT ARE ROUTINE AND EVERYBODY IS RUNNING THEM. AND SO IN THAT INSTANCE, DOES IT MAKE SENSE TO RE-INVENT THE WHEEL AND SPEND CIRM DOLLARS EVERY SINGLE TIME? COULD THERE BE SOMETHING THAT THEY COULD SHARE?

FOR PROPRIETARY ASSAYS LIKE THE ONE YOU MENTIONED, THERE'S TWO COMPONENTS THAT WE NEED TO BE CAREFUL OF. SO ON THE DATA SHARING PART, WE WANT TO MAKE SURE THAT ANY DATA SHARING REQUIREMENTS THAT WE PUT OUT FOR THIS PROGRAM ARE ULTIMATELY GOING TO BE

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SOMETHING WHERE THE SHARED DATA CAN BE USEFUL FOR PRECLINICAL DEVELOPMENT. SO WE REALLY WANT TO FOCUS ON THAT, FIND OUT HOW WE CAN DO THAT, AND DO IT WITHOUT JEOPARDIZING THE DEVELOPMENT OF ANY PARTICULAR THERAPEUTIC CANDIDATE. AND SO THAT PART IS SOMETHING WE'RE THINKING THROUGH.

IF, FOR EXAMPLE, THAT PARTICULAR ASSAY THAT DR. GOLDEN IS DEVELOPING COULD BE USEFUL FOR ANOTHER AWARDEE, WE MAY, FOR THE KNOWLEDGE NETWORK PART, TRY TO FACILITATE INTERACTION BETWEEN THOSE AWARDEES, RIGHT, WHERE IT MIGHT SENSE. NOW, WE'RE NOT SAYING THAT WE OURSELVES ARE GOING TO DISCLOSE THAT. WE WOULD HAVE TO GO THROUGH AND DISCUSS IT WITH BOTH AWARDEES IF IT MAKES SENSE FOR THEM TO COLLABORATE, COORDINATE, OR SHARE SOMEBODY'S. SO THAT'S HOW THE KNOWLEDGE NETWORK COMPONENT WILL COME INTO PLAY.

THE DATA SHARING REQUIREMENT IS GOING TO BE SOMETHING THAT WE CAREFULLY THINK THROUGH AS TO WHAT DATA CAN BE SHARED WITH THE ULTIMATE INTENT OF MAKING SURE THAT WHATEVER IS SHARED IS ACTUALLY USEFUL.

DR. LEVITT: OKAY. THAT'S IMPORTANT. AS YOU KNOW, YOU KNOW THIS BETTER THAN I, CLARIFYING THIS SO THAT INSTITUTIONS UNDERSTAND THAT WHEN

INVESTIGATORS SAY THIS IS PART OF WHAT OUR RESPONSIBILITY IS, THEY DON'T COMPLETELY LOSE IT AND SAY, NO, YOU CAN'T APPLY FOR THAT GRANT BECAUSE ALL THINGS HAVE TO BE HELD CLOSE TO THE VEST OR SOMETHING. SO THAT WILL HELP IN TERMS OF CLARIFICATION OF WHAT THE EXPECTATIONS ARE. AND CERTAINLY CIRM FACILITATING COLLABORATIONS, DID YOU KNOW THAT JEFF HAS THIS AMAZING ASSAY, YOU SHOULD TALK TO HIM ABOUT IT KIND OF A THING, RIGHT? IF THE INVESTIGATORS KNOW THAT THAT IS GOING TO BE PART OF THE PROCESS, I THINK THEY'LL BE ENCOURAGED BY THAT.

DR. PATEL: WE'RE ALSO THINKING ABOUT HAVING FOCUSED WORKSHOPS AROUND THIS PARTICULAR TOPIC THAT'S RELEVANT TO MULTIPLE AWARDEES INSTEAD OF DOING IT IN A SETTING WHERE IT'S JUST CIRM AWARDEES, MAYBE THEY'RE MORE WILLING TO PARTICIPATE AND COORDINATE THAT WAY.

DR. LEVITT: YEP.

DR. PATEL: I APPRECIATE THE COMMENT THAT YOU MADE IN DR. CHAN LEK TAN'S PRESENTATION AS WELL OF BEING VERY CLEAR ABOUT OUR EXPECTATIONS IN THE PA AND THE APPLICATION. SO THANK YOU FOR THAT.

MR. TOCHER: NOT SEEING ANY OTHER HANDS AT THE MOMENT, MARK.

MS. MANDAC: MARK, YOU SEEM TO BE ON MUTE.

MR. TOCHER: MARK, COULD YOU GIVE US AN AUDIO CHECK? I'M NOT HEARING YOU IF YOU'RE IN THE ROOM.

CHAIRMAN FISCHER-COLBRIE: SORRY ABOUT THAT. MY APOLOGIES. THAT NEVER HAPPENS. I DON'T KNOW WHAT HAPPENED.

ANY QUESTIONS FROM THE COMMITTEES BEFORE WE CLOSE THE CONVERSATION? ANY COMMENTS OR QUESTIONS FROM THE COMMITTEE?

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

CHAIRMAN FISCHER-COLBRIE: OKAY. GREAT. ANYBODY FROM THE PUBLIC, QUESTIONS OR COMMENTS?

MR. TOCHER: NO, DOESN'T APPEAR SO.

CHAIRMAN FISCHER-COLBRIE: OKAY. THANK YOU. WELL, LET'S GO AHEAD WITH THE ROLL CALL VOTE, SCOTT. THANK YOU.

MR. TOCHER: AND THE MOTION IS TO RECOMMEND TO THE ICOC APPROVAL OF THE PDEV CONCEPT PLAN.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: YES.

MR. TOCHER: LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: YES.

MR. TOCHER: DEBORAH DEAS.

DR. DEAS: YES.

MR. TOCHER: MARK FISCHER-COLBRIE.
CHAIRMAN FISCHER-COLBRIE: YES.
MR. TOCHER: ELENA FLOWERS.
DR. FLOWERS: YES.
MR. TOCHER: JUDY GASSON.
DR. GASSON: YES.
MR. TOCHER: JEFF GOLDEN.
DR. GOLDEN: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: YES.
MR. TOCHER: PAT LEVITT.
DR. LEVITT: YES.
MR. TOCHER: CAROLYN MELTZER.
DR. MELTZER: YES.
MR. TOCHER: CHRIS MIASKOWSKI.
DR. MIASKOWSKI: YES.
MR. TOCHER: MARV SOUTHARD.
DR. SOUTHARD: YES.
MR. TOCHER: KAROL WATSON.
DR. WATSON: YES.
MR. TOCHER: KEITH YAMAMOTO.
DR. YAMAMOTO: YES.
MR. TOCHER: THANK YOU VERY MUCH. MARK,

THE MOTION CARRIES UNANIMOUSLY.

DR. PATEL: THANK YOU.

VICE CHAIR BONNEVILLE: THANK YOU, SHYAM, SO MUCH.

DR. YAMAMOTO: GREAT JOB.

CHAIRMAN FISCHER-COLBRIE: THAT'S A LOT TO GO THROUGH. SO LET'S PROCEED.

MR. TOCHER: WE'RE ON THE HOME STRETCH NOW, MARK. AND WE'RE JUST SETTING UP HERE. STAND BY. WE'RE JUST GETTING THE PRESENTATION COMPUTER SET UP.

CHAIRMAN FISCHER-COLBRIE: NO PROBLEM.

DR. KADYK: OKAY. GOOD AFTERNOON, MEMBERS OF THE BOARD AND COLLEAGUES AND MEMBERS OF THE PUBLIC. MY NAME IS LISA KADYK. I'M A MEMBER OF THE CLINICAL DEVELOPMENT TEAM AT CIRM.

AND I'M HERE TO PRESENT TO YOU PROPOSED UPDATES TO THE CLIN2 CONCEPT. CLIN2 IS OUR FUNDING OPPORTUNITY FOR CLINICAL TRIAL STAGE AWARDS. AND MY PRESENTATION IS GOING TO FOLLOW THE SAME OUTLINE THAT YOU'VE SEEN FOR THE PREVIOUS CONCEPT PRESENTATIONS.

SO, AGAIN, THE CLIN2 UPDATE IS AGAIN RESPONSIVE TO GOAL 4 OF THE SAF THAT WAS APPROVED BY THE BOARD BACK IN SEPTEMBER. AND THAT GOAL IS TO

PROPEL 15 TO 20 THERAPIES TARGETING DISEASES AFFECTING CALIFORNIANS TO LATE STAGE TRIALS. AND THE UPDATES TO THE CLIN2 PROGRAM ARE TO ALLOW FOR SUPPORT OF EMERGING NOVEL CLINICAL TRIAL DESIGNS, INCENTIVIZE STAGE APPROPRIATE MARKET ACCESS STRATEGY DEVELOPMENT, AND PRECOMMERCIALIZATION ACTIVITIES, AND ALSO, AS FOR THE OTHER PROGRAMS, INCORPORATING PRIORITIZATION OF INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT CALIFORNIANS.

SO I'LL START WITH A LITTLE BIT OF BACKGROUND INFORMATION ABOUT SOME OF THE CHALLENGES AND OPPORTUNITIES THAT WE SEE IN OUR CLIN2 PROGRAM. TO START, THE CLINICAL DEVELOPMENT TEAM DID A DEEP DIVE ANALYSIS OF OUR EXISTING CLINICAL TRIAL DATASET, WHICH AT THE TIME WAS 110 CLINICAL TRIALS THAT HAS BEEN FUNDED BY CIRM. AND THIS INCLUDES BOTH ACTIVE AND CLOSED AWARDS. AND AS PART OF THAT ANALYSIS, WE IDENTIFIED A NUMBER OF CHALLENGES THAT SOMETIMES ARISE FOR OUR CLINICAL TRIAL AWARDS, INCLUDING DELAYS IN REACHING OPERATIONAL MILESTONES, LACK OF ADVANCEMENT TO THE NEXT PHASE CLINICAL TRIAL, LACK OF PARTNERSHIPS THAT COULD TAKE THE PROGRAM FORWARD TO NON-CIRM FUNDING, AND LACK OF EMPHASIS ON COMMERCIALIZATION PLANNING.

IN ADDITION, WE DID A STUDY OR WE READ A

STUDY THAT WAS DONE BAY IQVIA OF A BROADER LANDSCAPE ANALYSIS OF THE CELL AND GENE THERAPY FIELD. AND ONE IMPORTANT CONCLUSION FROM THAT STUDY WAS THAT 50 PERCENT OF MARKETED CELL AND GENE THERAPIES THAT ORIGINATE IN ACADEMIA OR EMERGING BIOPHARMA ARE LAUNCHED EVENTUALLY BY A LARGER COMPANY. AND, IN FACT, ACADEMIA AND EMERGING BIOPHARMA ARE CLIENTELE OF CLIN2 AWARDS. SO WE CONCLUDE THAT CIRM'S CLINICAL PROGRAMS WILL EVENTUALLY DEPEND ON PARTNERING FOR BLA AND COMMERCIALIZATION.

AND SO WE THINK THERE'S AN OPPORTUNITY NOW TO HELP OUR CLINICAL TRIAL AWARDS BE BETTER POSITIONED FOR PARTNERING AND FOR EVENTUAL BLA AND COMMERCIALIZATION. AND TOWARD THAT END, WE WANT TO MAKE SOME MODIFICATIONS TO THE EXISTING CLIN2 CONCEPT AND PROGRAM ANNOUNCEMENT TO ENCOURAGE EARLIER DEVELOPMENT OF CLINICAL AND MANUFACTURING STRATEGIES, TO HAVE A MARKET ACCESS STRATEGY, AND TO HAVE STAGE APPROPRIATE PRECOMMERCIALIZATION ACTIVITIES.

SO, AGAIN, THE OBJECTIVE OF THE CLIN2 AWARDS IS TO ACCELERATE CLINICAL DEVELOPMENT OF STEM CELL-BASED AND GENETIC THERAPIES TO LATE STAGE TRIALS BY ENCOURAGING INNOVATIVE CLINICAL TRIAL DESIGNS AND BY INCENTIVIZING STAGE APPROPRIATE

MARKET ACCESS ACTIVITIES AND PRECOMMERCIALIZATION ACTIVITIES.

SO I'M GOING TO START OUT WITH OUTLINING THE SCOPE OF THE CLIN2 PROGRAM. THIS IS, AGAIN, TO FUND PHASE 1, 2, OR 3 CLINICAL TRIALS, INCLUDING REGISTRATIONAL TRIALS USING A REGENERATIVE MEDICINE APPROACH, CELL AND GENE THERAPY-BASED APPROACHES. AND I'LL DISCUSS FIRST THE REQUIRED ELEMENTS AND ACTIVITIES OF A CLIN2 AWARD AS WELL AS, THEN, THE ALLOWABLE ACTIVITIES.

SO STARTING WITH THE REQUIRED ACTIVITIES, FIRST OF ALL, OF COURSE, WE DO EXPECT COMPLETION OF A CLINICAL TRIAL, BUT WE'RE ALSO GOING TO HIGHLIGHT GOING FORWARD THAT WE'RE ENCOURAGING THOSE THAT HAVE ACCELERATING CLINICAL TRIAL DESIGNS, SUCH AS BASKET TRIALS OR ADAPTIVE TRIAL DESIGNS. IN ADDITION, AND THIS IS NEW, WOULD BE THAT THE AWARDEE WOULD BE REQUIRED TO ESTABLISH A STRATEGIC PLANNING COMMITTEE. AND SO WHAT'S THAT? WE ENVISION THAT THAT WOULD BE COMPRISED OF EXPERTS WHO HAVE EXPERTISE IN BRINGING A CELL AND/OR GENE THERAPY ALL THE WAY TO BLA AND MARKETING SO THAT THEY HAVE EXPERTISE IN THE REGULATORY AND MANUFACTURING AND PRECOMMERCIALIZATION ACTIVITIES THAT ARE NEEDED AND WILL BE ABLE TO PROVIDE A REAL STRATEGIC AND

FORWARD-THINKING ADVICE TO OUR GRANTEES.

IN ADDITION, WE WANT TO NOW INCORPORATE A DATA SHARING REQUIREMENT IN THE CLIN2 AWARDS TO ENSURE THAT EVENTUALLY CLINICAL TRIAL DATA THAT CIRM'S FUNDED WILL BE FINDABLE AND ACCESSIBLE FOR THOSE WHO COULD BENEFIT FROM IT IN THE FUTURE.

WE WANT TO CONTINUE TO ENCOURAGE ALL OF OUR CLINICAL TRIALS TO HAVE APPROPRIATE OUTREACH THAT THEY CAN ENROLL A DEMOGRAPHIC POPULATION INTO THEIR TRIAL THAT MATCHES THE DEMOGRAPHICS OF THE DISEASE POPULATION AT LARGE.

AND FINALLY, WE'RE NOW ADDING A MUCH GREATER EMPHASIS, AS I MENTIONED EARLIER, ON STAGE APPROPRIATE COMMERCIALIZATION AND ACCESS AND AFFORDABILITY ACTIVITIES, ALL REQUIRED.

WE ALSO HAVE SOME OTHER ACTIVITIES THAT ARE ALLOWABLE, BUT NOT NECESSARILY REQUIRED. ONE OF WHICH IS WE WOULD FUND NATURAL HISTORY STUDIES THAT ARE FDA APPROVED THAT MAY BE NEEDED FOR BASELINE OR CONTROL DATA WHEN THAT STUDY IS BEING DONE IN CONJUNCTION WITH AN INTERVENTIONAL TRIAL FUNDED UNDER THAT SAME AWARD.

ALSO, WE WOULD ALLOW MANUFACTURING FOR THE NEXT PHASE TRIAL. WE HAVE ALWAYS ALLOWED THAT IN THE CLIN2 PROGRAM BECAUSE WE BELIEVE THAT IS AN

ACCELERATING ACTIVITY TO HAVE PRODUCT MADE FOR THE NEXT PHASE TRIAL IF THE PROGRAM IS MOVING ON. HOWEVER, WE WANT TO MAKE A WILL LITTLE TWEAK TO HOW THAT IS DONE AND HAVE THAT ACTIVITY -- INITIATION OF SUCH AN ACTIVITY, WHICH IS VERY EXPENSIVE ACTIVITY, NOW BE GATED ON AN EVALUATION OF THE CURRENT TRIAL DATA TO BE SURE THAT THE PROGRAM REALLY IS WARRANTED FOR THAT PROGRAM TO GO ON TO THE NEXT STAGE TRIAL AND ALSO GATED ON THE ABILITY OF THE AWARDEE TO PROVIDE 50 PERCENT CO-FUNDING FOR THAT MANUFACTURING ACTIVITY.

SO THIS IS JUST A REMINDER THAT ONE OF THE MANDATES FROM THE UPDATES FROM THE SAF GOAL 4 IS TO INCORPORATE PRIORITIZATION OF INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT CALIFORNIANS AS WAS MENTIONED, ALSO FOR THE PRECLINICAL DEVELOPMENT PROGRAM. AND SO I HAVE -- THIS IS ACTUALLY THE SAME SLIDE THAT DR. PATEL JUST RECENTLY WENT THROUGH IN MORE DETAIL FOR THE PRECLINICAL DEVELOPMENT PROGRAM. WE HAD THE SAME GUIDING PRINCIPLES AND AN IMPLEMENTATION PLAN FOR IDENTIFYING PREFERENCES THAT COULD BE USED GOING FORWARD FOR THE CLINICAL PROGRAM. AND WE WANTED THIS TO BE VERY MUCH IN ALIGNMENT WITH THE PRECLINICAL DEVELOPMENT PROGRAM.

SO ON THE NEXT SLIDE I'LL SHOW YOU THE

PREFERENCES THAT WE PROPOSE FOR CLIN2. AND YOU'LL SEE HERE ACTUALLY THE TOP HALF OF THE TABLE IS IDENTICAL TO THE TOP HALF OF THE PRECLINICAL DEVELOPMENT PREFERENCES RECOMMENDATIONS THAT DR. PATEL WENT THROUGH. SO THE FIRST THREE LINES ARE PREFERRED THERAPEUTIC MODALITIES THAT WE THINK CAN ADDRESS PATIENT ACCESS AND AFFORDABILITY BARRIERS. AND THE FOURTH LINE IS PRIORITIZING DISEASES OF THE BRAIN AND CNS, WHICH, OF COURSE, IS A PROP 14 PRIORITY.

IN ADDITION, DOWN IN THE BOTTOM HALF OF THE TABLE IN BOLD, ARE OTHER PREFERENCES THAT WE WANT TO PROPOSE TO BE SPECIFIC TO THE CLIN2 AWARD MECHANISM. THE FIRST BEING THAT WE WOULD GIVE PREFERENCE TO APPLICANTS WHO ARE CALIFORNIA-BASED ORGANIZATIONS SINCE, OF COURSE, THIS IS A CALIFORNIA TAXPAYER FUNDED INITIATIVE.

IN ADDITION, WE WOULD GIVE PREFERENCES TO PIPELINE IND-ENABLING STAGE OR PREVIOUS EARLIER CLINICAL TRIAL STAGE AWARDS.

WE WOULD GIVE PREFERENCE TO PROGRAMS THAT HAVE ALREADY RECEIVED RMAT OR FDA DESIGNATIONS FROM THE FDA WHICH ARE ACCELERATING TOWARDS BLA BECAUSE YOU GET GREATER FDA ACCESS WITH THOSE DESIGNATIONS.

AND FINALLY, WE WOULD GIVE PREFERENCE TO

ANY APPLICANT WHO'S PROPOSING A PIVOTAL TRIAL.

AND THESE ARE ALL OBJECTIVE PREFERENCES THAT COULD BE USED EITHER DURING THE PREREVIEW PROCESS OR IN THE APPLICATION REVIEW SUBCOMMITTEE OF THE BOARD.

OKAY. SO JUST TO MOVE ON TO THE STRUCTURE OF THE CLIN2 PROGRAM, THIS PROGRAM'S ACTUALLY STRUCTURE IS ALMOST IDENTICAL TO WHAT IT WAS BEFORE. SO I JUST HIGHLIGHTED IN BOLD A COUPLE OF DIFFERENCES THAT I WANT TO HIGHLIGHT TODAY. THE FIRST IS IN THE FIRST LINE WHICH IS THE RECURRENCE. WE'RE PROPOSING THAT THIS OPPORTUNITY BE OFFERED QUARTERLY INSTEAD OF MONTHLY AS IT WAS PREVIOUSLY. AND WE ALSO WANT TO CHANGE THE CO-FUNDING REQUIREMENTS FOR LATER PHASE TRIALS, PHASE 2 OR BEYOND, TO 50 PERCENT WHERE THEY PREVIOUSLY WERE 40 PERCENT. AND THIS IS IN LINE WITH OUR GOAL TO REALLY INCENTIVIZE INVESTMENT FROM PARTNERS FOR PROGRAMS THAT REALLY LOOK PROMISING TO GO ALL THE WAY TO BLA.

WE ARE GOING TO PROPOSE A BUDGET OF $135 MILLION FOR THE FIRST FISCAL YEAR, 25/26. AND THIS WAS PROPOSED BECAUSE WE FEEL LIKE IT CAN ENCOMPASS A VARIETY OF DIFFERENT SCENARIOS. AS YOU CAN SEE, WE HAVE DIFFERENT FUNDING CAPS FOR THE DIFFERENT PHASE

OF TRIALS. IF WE HAD ALL LATE STAGE TRIALS, AT ONE EXTREME WE COULD FUND UP TO NINE LATER PHASE TRIALS AT $15 MILLION EACH. HOWEVER, WE DO KNOW THAT HISTORICALLY CIRM HAS FUNDED -- 80 PERCENT OF THE TRIALS THAT WE FUND ARE FIRST IN HUMAN. SO THOSE HAVE LOWER PROJECT CAPS. SO WHEN YOU FACTOR THAT INTO ACCOUNT, WE EXPECT WE'LL HAVE A MIXTURE OF EARLY AND LATE STAGE TRIALS, AND WE THINK THAT WE COULD PROBABLY EASILY MEET OR EVEN SURPASS OUR HISTORICAL AVERAGE NUMBER OF CLINICAL TRIALS PER YEAR, WHICH IS THE FOOTNOTE DOWN HERE, HAS BEEN 13 TRIALS FUNDED PER YEAR IN THE PAST THREE YEARS.

SO HERE'S A SLIDE DESCRIBING THE ELIGIBILITY REQUIREMENTS FOR THE CLIN2 PROGRAM. AGAIN, THERE ARE NOT THAT MANY CHANGES FROM WHAT WE HAD HISTORICALLY. AND I JUST WANT TO HIGHLIGHT A COUPLE THAT ARE, AGAIN, SHOWN IN BOLD FONT HERE.

THE FIRST ONE IS IN THE CATEGORY OF CANDIDATE READINESS. CURRENTLY WE REQUIRE THAT, IN ORDER TO SUBMIT A CLIN2 APPLICATION TO CIRM, THE APPLICANT MUST HAVE ALREADY RECEIVED IND CLEARANCE FROM THE FDA. AND WE WANT TO MAINTAIN THAT REQUIREMENT FOR ANY NEW PROGRAMS TO CIRM. HOWEVER, FOR CIRM PIPELINE PROGRAMS, WE WANT TO GIVE THEM AN OPPORTUNITY, THE BEST POSSIBLE OPPORTUNITY FOR A

SMOOTH TRANSITION BETWEEN THE PRECLINICAL AND CLINICAL PHASE. AND SO IF THERE IS A CLIN2 APPLICATION DEADLINE COMING UP, WE WOULD ALLOW THEM TO SUBMIT THAT OPPORTUNITY ONCE THEY HAVE AN IND SUBMITTED TO THE FDA, BUT WE WOULD NOT REQUIRE THAT THEY'VE ALREADY RECEIVED FDA CLEARANCE AT THE TIME OF APPLICATION. WE WOULD STILL MAINTAIN THE REQUIREMENT THAT THE FDA HAS CLEARED THE IND BEFORE THE APPLICATION WOULD GO TO FULL GRANTS WORKING GROUP REVIEW.

AND THE OTHER MAJOR DIFFERENCE HERE WOULD BE JUST WE WANT TO CHANGE THE PERIOD OF TIME BETWEEN ICOC APPROVAL AND OFFICIAL LAUNCH DATE OF THE AWARD TO 60 DAYS. IT WAS PREVIOUSLY 45 DAYS. AND THIS IS JUST TO ALLOW MORE TIME FOR THE ADMINISTRATIVE ASPECTS OF LAUNCHING THE AWARD.

WITH RESPECT TO APPLICATION AND REVIEW, AGAIN, WE'RE LARGELY PROPOSING TO MAINTAIN THE SAME PREREVIEW PROCESS THAT HAS BEEN USED FOR CLIN2 IN THE PAST. AFTER APPLICATION SUBMISSION, THERE IS A PROCESS OF CHECKING FOR MEETING ALL THE ELIGIBILITY REQUIREMENTS. IN ADDITION, WE NOW WANT TO ADD A STEP WHERE WE WOULD CHECK FOR COMPLETENESS OF THE APPLICATION USING AN OBJECTIVE CHECKLIST TO MAKE SURE THAT ALL THE REQUIRED COMPONENTS ARE REALLY

THERE. AND ESPECIALLY WE WANT TO FOCUS ON SOME OF THE NEWER COMPONENTS OF THE APPLICATION, INCLUDING PATIENT ACCESS AND COMMERCIALIZATION COMPONENTS.

WE ALSO STILL WOULD MAINTAIN A PROCESS THAT COULD BE IMPLEMENTED IF THERE ARE HIGHER APPLICATION VOLUMES THAT COULD BE MANAGED IN A REVIEW -- IN A GIVEN REVIEW CYCLE. AND THIS IS WHERE THE PREFERENCES CAN BE APPLIED TO PRIORITIZE APPLICATIONS THAT WOULD GO TO FULL REVIEW.

WE DO WANT TO MAKE A CHANGE IN THE CURRENT SCORING SYSTEM. IT WAS PREVIOUSLY A TIER I, II, III SCORING SYSTEM. WE WANT TO NOW HAVE THE CLIN2 PROGRAM ADOPT A 1 TO 100 SCORING SYSTEM. AND THAT WOULD BE IN ALIGNMENT WITH ALL THE OTHER CIRM PROGRAMS, AND WE BELIEVE THIS WILL IMPROVE THE GRANULARITY AND VISIBILITY FOR SCORE-DRIVING DECISIONS.

AND I JUST WANT -- I MENTIONED THIS ON AN EARLIER SLIDE, THESE TWO POINTS, BUT I THINK THEY'RE WORTH REEMPHASIZING HERE, THAT WE ARE ADDING IN THESE NEW REQUIREMENTS FOR ACCESS AND AFFORDABILITY PLANNING STAGE APPROPRIATELY, INCLUDING COMMERCIALIZATION PLANNING, FOR ALL THE CLIN2 PROGRAMS. AND WE ALSO WANT TO IMPLEMENT A DATA SHARING AND MANAGEMENT PLAN IN COORDINATION WITH ALL

OF CIRM'S OTHER DATA SHARING INITIATIVES, AND THIS IS REALLY IMPORTANT FOR MAKING SURE THAT THOSE DATA THAT WE HAVE INVESTED IN CAN BE -- WE CAN MAXIMIZE THE VALUE OF THOSE DATA DOWN THE ROAD.

AND GETTING CLOSE TO THE END HERE. WE HAVE ALWAYS CONSIDERED OURSELVES PARTNERS WITH OUR GRANTEES, ESPECIALLY AT THE CLINICAL TRIAL STAGE. WE REALIZE THAT WE'RE INVESTING A LOT OF MONEY IN THESE PROGRAMS. AND AS SUCH, WE WANT TO MAXIMIZE THAT INVESTMENT AND HELP THEM AS MUCH AS POSSIBLE. PART OF THAT IS MAINTAINING A CLOSE RELATIONSHIP WITH ALL OUR GRANTEES. SO WE WANT TO MAINTAIN OUR CURRENT REQUIREMENT TO HAVE THEM SUBMIT QUARTERLY PROGRESS REPORTS. AND THEN WE WOULD HAVE FOLLOW-UP WITH CALLS WITH THEM AS NEEDED, WHICH WE NORMALLY DO. WE WANT TO REINFORCE THE CURRENT REQUIREMENT THAT CIRM BE INCLUDED IN ANY INTERACTIONS WITH THE FDA, INCLUDING MEETINGS WITH THE FDA. AND WE WOULD ALSO WANT CIRM TO BE INCLUDED IN ANY MEETINGS WITH THE NEW STRATEGIC PLANNING COMMITTEES THAT WE ARE GOING TO BE REQUIRING.

AND WE DO STILL HAVE ENFORCEMENT AT THE FISCAL LEVEL. WE HAVE, AS DR. PATEL OUTLINED, OPERATIONAL MILESTONE-DRIVEN AWARDS. AND IN THE CASE WHERE A GRANTEE IS NOT ABLE TO REACH A

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OPERATIONAL MILESTONE AND THEY'VE EXHAUSTED THE CIRM FUNDING TRANCHE, THEY NEED TO HAVE CONTINGENCY FUNDING IN PLACE IN ORDER TO REACH THE MILESTONE BEFORE THEY WILL RECEIVE THE NEXT CIRM FUNDING TRANCHE.

AND IN ADDITION, BEFORE ANY AWARDS THAT HAVE A DELAY OF MORE THAN FOUR MONTHS OF REACHING A MILESTONE, THAT WOULD TRIGGER AN EVALUATION OF THE FEASIBILITY OF THIS PROGRAM REALLY BEING ABLE TO CONTINUE WITH THE RIGHT TO TERMINATE THE AWARD. AND WE WOULDN'T TAKE IT LIGHTLY TO TERMINATE AN AWARD THAT WE'VE ALREADY INVESTED A LOT IN, AND WE WOULD CERTAINLY WISH TO MAXIMIZE OUR EFFORT TO HELP THEM BE SUCCESSFUL.

SO I JUST WANT TO END WITH A PROPOSED TIMELINE FOR RELAUNCHING THE CLIN2 PROGRAMS. IF THIS CONCEPT IS APPROVED AT THE BOARD AT THE END OF MARCH, WE WOULD PROPOSE TO HAVE APPLICATIONS OPEN BY MID-MAY, APPLICATION DEADLINES IN JULY, FIRST GRANTS WORKING GROUP IN SEPTEMBER, AND COMING TO THE BOARD FOR APPROVALS IN NOVEMBER. AND THEN YOU CAN SEE ON THIS NEXT LINE DOWN THAT WE WOULD HAVE ANOTHER CYCLE STARTING IN EARLY AUGUST.

SO IN CONCLUSION, WE WOULD HAVE THE FIRST CYCLE OF NEW CLIN2 AWARDS WOULD BE LAUNCHING IN

FEBRUARY OF 2026.

AND WITH THAT, I'D LIKE TO CONCLUDE BY REQUESTING A MOTION THAT THE SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE RECOMMEND APPROVAL TO THE FULL ICOC OF THE CLIN2 CONCEPT.

CHAIRMAN FISCHER-COLBRIE: GREAT. EXCELLENT PRESENTATION. THANK YOU. AND WITH THAT, I'D LIKE TO REQUEST FOR A MOTION AND A SECOND.

DR. HIGGINS: I'D LIKE TO MAKE A MOTION. THIS IS DAVID FROM SAN DIEGO.

DR. GASSON: I'LL SECOND. THIS IS JUDY.

CHAIRMAN FISCHER-COLBRIE: GREAT. WITH THAT, LET'S OPEN IT UP TO THE COMMITTEES FOR QUESTIONS AND COMMENTS.

MR. TOCHER: I DON'T SEE ANY HANDS AT THE MOMENT.

CHAIRMAN FISCHER-COLBRIE: OKAY. WITH THAT, I WOULD LIKE TO ASK IF THERE ARE ANY QUESTIONS OR COMMENTS FROM THE PUBLIC.

MR. TOCHER: WE DON'T SEE ANY HANDS RAISED, MARK.

DR. YAMAMOTO: ACTUALLY --

CHAIRMAN FISCHER-COLBRIE: WITH THAT -- KEITH, I THINK YOU JUST RAISED A HAND. GO AHEAD. FIRE AWAY.

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DR. YAMAMOTO: YEAH. THIS IS PROBABLY NOT -- I LIKE THIS PROPOSAL A LOT. I'M ABSOLUTELY GOING TO VOTE IN FAVOR OF IT. AND IT'S PROBABLY NOT RELEVANT TO RAISE THIS POINT HERE, BETTER TO WAIT FOR GIL'S PRESENTATION AT THE NEXT BOARD MEETING. BUT I REALLY DO FEEL OBLIGATED TO GO ON RECORD OPPOSING THIS NOTION OF A 1 TO 100 SCORING SYSTEM.

I KNOW THAT IT IS -- IN DISCLOSURE, I WAS BEHIND A MOVE TO MOVE THE NIH AWAY, 25 YEARS AGO, AWAY FROM THE 1 TO 100 SCALE. IT PRESENTS THE ILLUSION OF GRANULARITY THAT RATIONALIZES THESE FUNDING DECISIONS. BUT I THINK WE SHOULD ALL BE AWARE THAT IT'S AN ILLUSION, THAT NO SINGLE REVIEWER CAN REALLY DISTINGUISH BETWEEN A 26 AND A 27. AND CERTAINLY NO GROUP OF REVIEWERS WHO INDIVIDUALLY EVALUATE THINGS DIFFERENTLY ARE GOING TO BE ABLE TO RATIONALIZE THE DIFFERENCE BETWEEN 26 AND 27 WHEN THE SCORES GET AVERAGED.

AND SO IT JUST REALLY DOESN'T -- IT'S A FALSE ILLUSION OF CAPACITY FOR QUANTITATIVE GRANULARITY. AND IT'S MUCH BETTER WE MOVE TO A DIGITAL SYSTEM BETWEEN A 1 AND 9. AND HUMANS HAVE A HARD ENOUGH TIME DISTINGUISHING BETWEEN NINE DIFFERENT GRADATIONS OF QUALITY. BUT IT'S MUCH BETTER THAN THIS ILLUSION OF LETS GO OUT TO THREE

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DECIMAL PLACES AND BE ABLE TO SAY, WELL, THIS GRANT IS CLEARLY BETTER THAN THE OTHER ONE BECAUSE IT'S A THOUSANDTH OF A POINT BETTER IN AN AVERAGE SCORE.

SO I REALLY THINK IT'S A MISTAKE. IT'S SOMETHING THAT I'LL TALK A LOT -- I'LL TALK ABOUT MORE ACTUALLY WITH GIL OFFLINE, BUT I WANTED TO JUST GO ON RECORD SAYING THAT I THINK THERE'S A CONCERN THERE. I THINK THIS PROPOSAL ITSELF IS VERY GOOD, AND I'M STRONGLY IN FAVOR OF IT.

CHAIRMAN FISCHER-COLBRIE: GREAT COMMENT, KEITH. AND IT'S GREAT TO BE ABLE TO TAKE ADVANTAGE OF YOUR DIRECT EXPERTISE HERE. AND I THINK IT POINTS TO THE FACT THAT THERE'S STILL REVIEWS THAT NEED TO BE WRAPPED UP AHEAD THE MARCH BOARD MEETING TO ENSURE THAT WE'RE ON THE BEST COURSE POSSIBLE RELATED TO THE MARCH PRESENTATION. SO YOUR COMMENTS ARE WELL TAKEN AND WELL NOTED. REALLY APPRECIATE IT.

OTHER QUESTIONS OR COMMENTS BEFORE WE DO THE ROLL CALL VOTE?

MR. TOCHER: I DON'T SEE ANY HANDS, MARK. SO WILL I'LL PROCEED WITH THE ROLL CALL. SO THE MOTION IS TO RECOMMEND TO THE BOARD APPROVAL OF THE CLIN2 CONCEPT.

MARIA BONNEVILLE.

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VICE CHAIR BONNEVILLE: YES.
MR. TOCHER: LEONDRA CLARK-HARVEY.
DR. CLARK-HARVEY: YES.
MR. TOCHER: DEBORAH DEAS. MARK FISCHER-COLBRIE.
CHAIRMAN FISCHER-COLBRIE: YES.
MR. TOCHER: ELENA FLOWERS.
DR. FLOWERS: YES.
MR. TOCHER: JUDY GASSON.
DR. GASSON: YES.
MR. TOCHER: JEFF GOLDEN.
DR. GOLDEN: YES.
MR. TOCHER: DAVID HIGGINS.
DR. HIGGINS: YES.
MR. TOCHER: VITO IMBASCIANI.
CHAIRMAN IMBASCIANI: YES.
MR. TOCHER: CAROLYN MELTZER.
DR. MELTZER: YES.
MR. TOCHER: CHRIS MIASKOWSKI.
DR. MIASKOWSKI: YES.
MR. TOCHER: MARV SOUTHARD. KAROL WATSON.
DR. WATSON: YES.
MR. TOCHER: KEITH YAMAMOTO.
DR. YAMAMOTO: YES.
MR. TOCHER: MARV, I THINK WE DIDN'T HEAR

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YOUR VOTE.

DR. SOUTHARD: I SAID YES.

MR. TOCHER: GREAT. WE GOT THAT LOUD AND CLEAR. THANKS VERY MUCH. AND THE MOTION CARRIES UNANIMOUSLY, MARK.

CHAIRMAN FISCHER-COLBRIE: OKAY. I THINK THAT CONCLUDES OUR MEETING IF I'M NOT MISTAKEN. SO IT'S A LOT OF MATERIAL HERE. I WOULD ENCOURAGE ONGOING CONVERSATIONS AND DIALOGUE, BUT THIS CONTINUES TO TAKE GREAT SHAPE AND FORM HERE WITH SOME OPEN QUESTIONS STILL TO GET RESOLVED AND CLARIFIED AS WE MOVE FORWARD. BUT CERTAINLY CONTINUED TREMENDOUS PROGRESS, ESPECIALLY GIVEN TIGHT TIMELINES AND SCHEDULES AND EXISTING COMMITMENTS OF KEEPING THINGS RUNNING WHILE THIS PROCESS HAS BEEN UNDER WAY. SO, AGAIN, KUDOS TO THE TEAM FOR THEIR EXTRAORDINARY EFFORTS IN THIS PROCESS. AND WE LOOK FORWARD TO GETTING THIS ACROSS THE GOAL LINE PRIMARILY IN MARCH AND THEN, OF COURSE, IN JUNE AS WELL. THANK YOU VERY MUCH.

DR. THOMAS: THANK YOU, MARK, AND COMMITTEE.

CHAIRMAN FISCHER-COLBRIE: GREAT. WITH THAT, UNLESS THERE'S ANY OTHER COMMENTS, I THINK WE'LL TURN THE TIME BACK TO EVERYONE AND WE CAN MOVE

FORWARD WITH OTHER ACTIVITIES.

MR. TOCHER: GREAT. THANKS VERY MUCH, MARK.

VICE CHAIR BONNEVILLE: THANKS, EVERYONE.

(THE MEETING WAS THEN CONCLUDED AT 3:15 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 JOINT MEETING OF THE SCIENCE SUBCOMMITTEE AND TASK FORCE ON NEUROSCIENCE AND MEDICINE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON MARCH 5, 2025, 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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