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

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: AUGUST 16. 2024
11:30 A.M.

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

FILE NO.: 2024-33

I N D E X

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

AUGUST 16, 2024; 11:30 A.M.

CHAIRMAN FISCHER-COLBRIE: LET'S CALL THE MEETING TO ORDER FOR THE SCIENCE SUBCOMMITTEE AND THE NEURO TASK FORCE WHERE YOU'VE JOINED TODAY. WITH THAT, I'D LIKE TO TURN IT OVER TO SCOTT TO CALL THE ROLL.

MR. TOCHER: SURE. THANK YOU, MARK.

MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MR. TOCHER: LEONDRA CLARK-HARVEY. MONICA CARSON.

DR. CARSON: HERE.

MR. TOCHER: MARK FISCHER-COLBRIE.

CHAIRMAN FISCHER-COLBRIE: HERE.

MR. TOCHER: FRED FISHER. FRED, PERHAPS YOU'RE ON MUTE. HE'S NOT IN THE ROOM. I'LL COME BACK.

ELENA FLOWERS.

DR. FLOWERS: PRESENT.

MR. TOCHER: JUDY GASSON. DAVID HIGGINS.

DR. HIGGINS: PRESENT.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: PRESENT.

MR. TOCHER: PAT LEVITT. SHLOMO MELMED.

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

DR. MELMED: PRESENT.

MR. TOCHER: CAROLYN MELTZER.

DR. MELTZER: PRESENT.

MR. TOCHER: CHRIS MIASKOWSKI.

DR. MIASKOWSKI: PRESENT.

MR. TOCHER: LAUREN MILLER-ROGEN. MARV SOUTHARD. KAROL WATSON.

DR. WATSON: PRESENT.

MR. TOCHER: FRED FISHER.

DR. FISHER: YES, I'M HERE.

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

CHAIRMAN FISCHER-COLBRIE: THANKS, SCOTT. AND WITH THAT, I'D LIKE TO TURN THE MEETING OVER TO IT J.T.

DR. THOMAS: THANKS, MARK. GOOD MORNING, EVERYBODY. AS YOU KNOW, WE'VE BEEN IN THE PROCESS SINCE LATE LAST YEAR ACTUALLY OF DETERMINING HOW BEST TO DEPLOY THE REMAINING $3.8 BILLION IN CIRM FUNDING AUTHORIZED BY PROP 14. AND TOWARDS THAT EFFORT, WE'VE BEEN ENGAGED IN A VERY EXTENSIVE PROCESS WHICH WE CALL THE STRATEGIC ALLOCATION FRAMEWORK TO DERIVE A SET OF GOALS AND RECOMMENDATIONS FOR THE BOARD TO CONSIDER ULTIMATELY AT OUR SEPTEMBER BOARD MEETING.

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

THAT PROCESS HAS INVOLVED A GREAT MANY MEETINGS ALONG THE WAY WITH VARIOUS MEMBERS OF THE SCIENCE SUBCOMMITTEE AND THE NEURO TASK FORCE AND HAS TAKEN ALL OF THAT INPUT AND INCORPORATED IT INTO THE EVOLVING PRODUCT THAT WE'RE PUTTING TOGETHER FOR ULTIMATE CONSIDERATION IN SEPTEMBER.

ROSA HAS MOST ABLY LED THIS EFFORT ON BEHALF OF THE TEAM, WHICH VIRTUALLY EVERY MEMBER OF CIRM HAS A PART OR HAS HAD A PART IN PUTTING THINGS TOGETHER TO GET US TO THIS POINT AND WHICH WILL BE INVOLVED IN GETTING US THROUGH THE FINISH LINE IN SEPTEMBER.

SO TODAY'S MEETING IS THE LATEST IN THE SERIES WITH HERE THE JOINT NEURO TASK FORCE AND SCIENCE SUBCOMMITTEE. WE'RE GREATLY LOOKING FORWARD TO YOUR INPUT. AND I WILL TURN THINGS NOW OVER TO ROSA TO GIVE THE PRESENTATION ON THIS LATEST SET OF GOALS AND RECOMMENDATIONS. ROSA.

DR. CANET-AVILES: THANK YOU, J.T. AND I WANT TO THANK THE CO-CHAIRS OF THE NEURO TASK FORCE, DR. CAROLYN MELTZER AND DR. PAT LEVITT AS WELL AS THE CHAIR OF THE SCIENCE SUBCOMMITTEE, DR. MARK FISCHER-COLBRIE, FOR THEIR SUPPORT AND HELP IN DEVELOPING THESE GOALS.

AND AS I GO TOWARDS SHARING, LET ME KNOW.

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

CAN YOU SEE THE PRESENTATION?

MR. MELTZER: YES, WE CAN.

DR. CANET-AVILES: I ALSO WANT TO ESPECIALLY THANK DR. ABLA CREASEY AND DR. SHYAM PATEL WHO HAVE BEEN INTEGRALLY INVOLVED IN THE DEVELOPMENT OF THESE TWO GOALS AS MEMBERS OF THE LEADERSHIP TEAM.

SO WITH LESS PREAMBLE, ON BEHALF OF CIRM, AND THAT MEANS A LOT OF MEMBERS OF OUR TEAM, I'LL BE PRESENTING TODAY'S PRESENTATION. AND TO ENSURE AMPLE TIME FOR DISCUSSION, THE BACKGROUND AND THE STRATEGIC ALLOCATION FRAMEWORK OVERVIEW WILL NOT BE PRESENTED DURING TODAY'S MEETING. AS A REFERENCE, THESE SECTIONS WERE PREVIOUSLY PRESENTED AT THE JUNE 27TH AND JULY 11TH MEETING. AND YOU HAVE A COUPLE OF LINKS IN THE PRESENTATION. SO YOU CAN GO TO THE YOUTUBE CIRM VIDEO TO GET INTO THOSE LINKS DIRECTLY AT THE POINTS OF THIS PRESENTATION.

SO DURING TODAY'S PRESENTATION, WE WILL GO OVER A QUICK REVIEW OF GOALS 1 AND 2 THAT WERE PRESENTED BACK IN JULY 11TH. AND THESE CORRESPOND TO THE CATEGORY OF ACCELERATING DISCOVERY AND TRANSLATION PIPELINE. AND WE'LL PRESENT THE FEEDBACK THAT WAS INCORPORATED FROM THE JULY MEETING, SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE

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

JOINT MEETING. WE WILL THEN PROCEED TO GO OVER GOALS 3 AND 4, CORRESPONDING TO CATEGORY OF CELL AND GENE THERAPY APPROVALS. AND THAT WILL BE FOLLOWED BY A DISCUSSION ON NEXT STEPS.

FEEL FREE TO INTERRUPT ME IF YOU HAVE ANY QUESTIONS. SO THIS IS JUST THE SLIDE TO SAY WHERE ARE WE. AND YOU CAN ALWAYS LOOK AT IT ON THE TOP RIGHT PART OF THE SLIDES. IT'S A GUIDANCE OF WHERE WE ARE. SO NOW WE ARE ON GOALS 1 AND 2.

SO AS A REMINDER HERE OF THE TWO FIRST GOALS PERTAINING TO THE FIRST CATEGORY, AT THE JOINT MEETING OF THE SCIENCE SUBCOMMITTEE AND NEURO TASK FORCE RECOMMENDATIONS, WE PROVIDED RECOMMENDATIONS FOR THOSE TWO GOALS. AND THOSE RECOMMENDATIONS WERE MET WITH STRONG APPROVAL, NOT FORMAL APPROVAL, BUT THERE WAS AGREEMENT WITH THOSE GOALS. AND THE BOARD MEMBERS NOT ONLY APPRECIATED THE THOROUGHNESS OF OUR INITIAL PROPOSAL, BUT ALSO PROVIDED VERY INSIGHTFUL FEEDBACK THAT HAS BEEN SINCE INCORPORATED INTO OUR UPDATED RECOMMENDATIONS.

SO WITH REGARDS TO THIS FIRST GOAL, THERE WERE TWO RECOMMENDATIONS. THE FIRST RECOMMENDATION WAS TO SUPPORT COMPREHENSIVE DISCOVERY RESEARCH THROUGH STRUCTURED INITIATIVES LIKE THE DISC4 AND DISC5 PILOT PROGRAMS THAT WE'VE JUST STARTED THIS

YEAR. WE'VE HAD THE FIRST OF THEM FOCUSED ON NEUROPSYCHIATRIC DISEASES. AND THAT'S THE DISC4, AKA REMIND, WHEN WE TALK ABOUT NEUROPSYCHIATRIC.

AND THE APPROACH IS TO ENCOURAGE COLLABORATIVE, MULTIDISCIPLINARY INNOVATION IN STEM CELL AND GENETIC RESEARCH ACROSS DIVERSE DISCIPLINES AND DISEASE INDICATIONS. AND THE BOARD UNDERSCORED THE IMPORTANCE OF ENSURING THAT THE RESEARCH FINDINGS ARE REPRODUCIBLE, PARTICULARLY WHEN TRANSITIONING DISCOVERIES FROM ACADEMIA TO INDUSTRY. AND THEY RECOMMENDED THAT WE ENGAGE INDUSTRY EARLY IN THE RESEARCH PROCESS TO HELP ADDRESS ISSUES OF REPRODUCIBILITY AND SCALABILITY. THIS IS CRITICAL FOR THE SUCCESSFUL TRANSLATION OF THIS FINDING INTO APPLICATIONS.

THE SECOND RECOMMENDATION HAD TO DO WITH DATA SCIENCE COLLABORATIVE EFFORTS. WE RECOMMENDED TO ESTABLISH A DATA COORDINATING AND MANAGEMENT CENTER TO STREAMLINE THE MANAGEMENT OF DATA TO ENHANCE THE UTILITY OF CROSS-DISEASE DATA. AND THE APPROACH WOULD BE TO BE FUND AND DEVELOP A CENTRAL HUB DATA COORDINATION, FACILITATING BETTER INTEGRATION WITH CONSORTIA AND RESEARCH INITIATIVES. AND THE BOARD SUPPORTED THE IDEA OF ESTABLISHING THESE CMC. AND THE INITIATIVE COULD ALSO ENHANCE

THE REPRODUCIBILITY AND VALIDATION OF SOME OF THE RESULTS FUNDED THROUGH CIRM, WHICH IS PIVOTAL TO MOVE RESEARCH FORWARD. BUT THE BOARD ALSO SUGGESTED THAT WE EXPLORE THE POTENTIAL FOR DEDICATED DATA SCIENCE GRANTS TO ENABLE THESE COLLABORATIVE EFFORTS.

AND THIS COULD BE AIMED TO LEVERAGING THE VAST DATASETS MANAGED BY THE PROPOSED CMC TO MAXIMIZE THE UTILITY OF WHAT WE ARE FUNDING. SO THIS FEEDBACK WILL BE FULLY INCORPORATED AND DELINEATED INTO THE SPECIFIC GRANULARITY OF THE CONCEPTS IF THE BOARD APPROVES THESE RECOMMENDATIONS AT THE SEPTEMBER BOARD MEETING.

THE SECOND GOAL UNDER THE FIRST CATEGORY, WHICH IS DISCOVERY AND TRANSLATIONAL THERAPIES, IS TO ACCELERATE THE DEVELOPMENT AND UTILIZATION OF X TECHNOLOGIES THAT DEMONSTRATE IMPROVEMENTS IN SAFETY, EFFICACY, AND QUALITY OF CELL AND GENE THERAPIES. AND THE CIRM TEAM RECOMMENDED TO PILOT AN INFRASTRUCTURE TECHNOLOGY PROGRAM TO BRIDGE THE GAP BETWEEN RESEARCH AND COMMERCIALIZATION BY FOSTERING PARTNERSHIPS BETWEEN ACADEMIC RESEARCHERS AND INDUSTRY PROFESSIONALS.

AND THE APPROACH COULD BE TO SUPPORT MULTISTAKEHOLDER TECHNOLOGY INCUBATION PROGRAMS TO

ACHIEVE DEFINED TECHNOLOGY READINESS LEVELS WHICH COULD FACILITATE THEN THE RAPID APPLICATION OF CELL AND GENE THERAPIES. AND THE FEEDBACK RECEIVED REGARDING THIS INFRASTRUCTURE TECHNOLOGY PLATFORM EMPHASIZE THE IMPORTANCE OF FOSTERING INDUSTRY/ ACADEMIC COLLABORATIONS AS WELL. SO, AGAIN, IT'S THE SAME TOPIC, BUT I THINK WE ARE SEEING A VERY COMMON THEME. AND IN THIS CASE COULD BE TO REFINE, SCALE, AND COMMERCIALIZE THE NEW TECHNOLOGIES.

AND THE BOARD FEEDBACK HIGHLIGHTED THAT DIFFERENT TYPES OF INDUSTRY PLAYERS, INCLUDING SMALL TECHNOLOGY INNOVATORS AND LARGE BIOPHARMA COMPANIES, COULD PLAY COMPLEMENTARY AND CRUCIAL ROLES IN THIS EFFORT. SO WE WILL BE ALSO INCORPORATING THIS INTO THE CONCEPT FOR YOUR CONSIDERATION IF THESE GOALS OBVIOUSLY RECOMMENDATION IS APPROVED IN SEPTEMBER.

SO BEFORE I GO INTO ANY QUESTIONS BECAUSE THIS PERTAINS TO GOAL 1 AND 2, WOULD YOU LIKE TO STOP FOR QUESTIONS HERE, OR WE JUST GO TO THE END, SCOTT? SORRY, I SHOULD ASK MARK. I'M SORRY.

CHAIRMAN FISCHER-COLBRIE: I THINK IT WOULD BE HELPFUL TO CONTINUE WITH THE DISCUSSION UNLESS THERE'S OTHER THOUGHTS.

DR. CANET-AVILES: SOUNDS GOOD. SO I'LL KEEP GOING. IF ANYBODY RAISES A HAND, I CAN STOP.

THANK YOU, MARK.

SO AS WE CONTINUE TO DRIVE INNOVATION WITHIN REGENERATIVE MEDICINE, ONE OF THE MAJOR GOALS THAT CIRM FACES IS THE WIDE SPECTRUM OF DISEASES FROM RARE TO COMMON. AND THIS IS IN THE CONTEXT OF CELL AND GENE THERAPY APPROVALS, THE GOALS FOR CELL AND GENE THERAPY APPROVALS. AND FOR THIS, WE HAVE DEVELOPED TWO GOALS.

HISTORICALLY OUR EFFORTS HAVE PREDOMINANTLY TARGETED RARE DISEASES, WHICH HAS ALLOWED US TO MAKE SIGNIFICANT STRIDES IN AREAS THAT OFTEN LACK ATTENTION AND FUNDING. BY CONCENTRATING IN THESE CONDITIONS, CIRM HAS ACTUALLY CATALYZED ADVANCEMENTS IN THE TRANSLATION OF THESE FINDINGS INTO CLINICAL APPLICATIONS AT A TIME. WHEN IT WAS TIME TO DO IT, THE FIELD WAS READY TO DO THIS IN RARE DISEASES. AND WE ARE AT A POINT WHERE THE LARGEST PROPORTION OF THE PROJECTS THAT WILL BE READY TO BLA IN THE NEXT TWO TO FOUR YEARS CORRESPOND TO THERAPIES TARGETING RARE AND ULTRA-RARE DISEASES IN OUR PORTFOLIO, IN CIRM'S PORTFOLIO.

SO IN THIS SLIDE WE ALIGNED OUR PRELIMINARY GOALS 3 AND 4, WHICH ARE GEARED TOWARDS NOT JUST MAINTAINING, BUT ACCELERATING THIS MOMENTUM

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

AND FINDING OPPORTUNITIES FOR OUR POPULATION IN CALIFORNIA. THE TWO GOALS THAT WE HAVE DEVELOPED FOCUS ON, FIRST, ADVANCE RARE DISEASE PROJECTS TO BLA BY LEVERAGING GENETIC TECHNOLOGIES, SCALING TO RARE DISEASES, FOR EXAMPLE, AND REGULATORY INNOVATION.

THIS GOAL WILL PROPOSE RECOMMENDATIONS FOR ACTIVITIES THAT WILL RESULT IN ADVANCING THERAPIES FOR RARE DISEASES TO REACH BLA AND PLACING ALL THE THERAPIES IN AN ACCELERATED PATH TOWARDS BLA.

FOR THE FOURTH GOAL, ON THE OTHER HAND, WE SEEK TO PROPEL THERAPIES TARGETING DISEASES THAT SIGNIFICANTLY AFFECT CALIFORNIANS TO LATE-STAGE TRIALS. AND THE OBJECTIVE IS TO ACCELERATE THE TIMELINE TO LATER STAGE CLINICAL DEVELOPMENT FOR THERAPIES THAT TARGET DISEASES AFFECTING CALIFORNIANS.

SO WE'VE DONE A LOT ON OF WORK TO GET TO THOSE RECOMMENDATIONS. SO WE ARE GOING TO DELVE NOW INTO THE DATA AND THE PROCESS THAT WE FOLLOWED TO MAKE RECOMMENDATIONS TO ACHIEVE THESE GOALS.

SO WE WILL GO OVER THE HIGH LEVEL QUESTIONS THAT WE CONSIDERED FOR EACH ONE OF THESE GOALS. SO THOSE QUESTIONS WERE THE QUESTIONS THAT A LARGE TEAM HAMMERED DOWN AND WITH FEEDBACK FROM

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

MEMBERS OF THE SCIENCE SUBCOMMITTEE AND THE NEURO TASK FORCE OVER THE PAST MONTH. AND THAT WITH ANSWERING THOSE QUESTIONS, WE THINK THAT WE COULD THEN MAKE SOME RECOMMENDATIONS. AND THEN WE'LL PRESENT A DATA AND ANALYSIS, AND THEN THE RECOMMENDATIONS, AND THEN WE WILL HAVE A DISCUSSION.

SO AS A REMINDER, THE GOAL IS TO ADVANCE AT LEAST X RARE DISEASE PROJECTS TO BLA. AND THE HIGH LEVEL QUESTIONS THAT WE WENT THROUGH WERE WITH REGARDS TO THE CURRENT PORTFOLIO, THE PURPOSE HERE OF THESE QUESTIONS WAS TO ASSESS THE ALIGNMENT OF OUR EXISTING PROJECTS WITH OUR RARE DISEASE OBJECTIVES AND TO FORECAST THE POTENTIAL IMPACT ON CIRM'S FUNDING.

THE SECOND TYPE OF QUESTIONS WERE ABOUT INFRASTRUCTURE UTILIZATION. HERE WAS THE FOCUS TO MAXIMIZE THE UTILITY OF OUR CURRENT INFRASTRUCTURE WHILE IDENTIFYING ANY NEW INVESTMENTS NEEDED TO OVERCOME UNIQUE CHALLENGES IN THERAPY DEVELOPMENT, IN RARE THERAPY DEVELOPMENT IN THIS CASE.

IN TERMS OF APPROACH, HERE WE EXPLORED THE MECHANISMS. WHAT ARE THE POTENTIAL STRATEGIES AND METHODOLOGIES THAT CAN DRIVE THE SUCCESSFUL DEVELOPMENT AND DELIVERY OF THESE RARE DISEASE THERAPIES?

AND LASTLY, WE THOUGHT ABOUT PARTNERSHIPS. WHAT KIND OF COLLABORATIONS, IF ANY, DO WE NEED TO IDENTIFY AND ENGAGE WITH IN ORDER TO ACCELERATE THE DEVELOPMENT AND APPROVAL PROCESS FOR THESE RARE THERAPIES?

FOR GOAL 4, WHICH IS TO PROPEL X THERAPIES TARGETING DISEASES AFFECTING CALIFORNIANS TO LATER STAGE TRIALS. THE TYPE OF QUESTIONS, AGAIN, WERE ABOUT DISEASE IMPACT. WHAT DISEASES ARE RELEVANT TO THE CALIFORNIA POPULATIONS AND AMENABLE TO CELL AND GENE THERAPIES? WHAT ARE THE CHALLENGES? IF NOT, ARE THERE ANY CHALLENGES THAT WE CAN OVERCOME BASED ON CELL AND GENE THERAPY RESEARCH TO MOVE THIS RESEARCH FORWARD?

IN TERMS OF THE CURRENT PORTFOLIO, SAME AS BEFORE. WE NEED TO ASSESS THE CURRENT STATE OF OUR PORTFOLIO WITH REGARDS TO THESE POTENTIAL DISEASES AND PARTICULARLY IN TERMS OF ITS RELEVANT TO CALIFORNIA HEALTH CONCERNS, AND IDENTIFY BARRIERS THAT MIGHT BE IMPEDING THE PROGRESS AND OPPORTUNITIES, AND THEN MAP THESE TO THE RECOMMENDATIONS.

IN TERMS OF APPROACH, THE QUESTION WAS TO REFINE ALSO OUR APPROACH TO FUND AND SUPPORT THESE TYPE OF PROJECTS.

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

AND THEN PARTNERSHIPS, THE SAME THING. DO WE NEED TO EXPLORE POTENTIAL NEEDS FOR PARTNERSHIPS? AND WHAT TYPES MIGHT BE MOST BENEFICIAL IN HELPING US MOVE THERAPIES THROUGH LATER STAGE TRIAL PIPELINE.

WE PRESENTED THIS SLIDE BACK WHEN WE PRESENTED THE JULY 11TH GOALS 1 AND 2, BUT I WILL GO ALSO IN DETAIL HERE FOR THE BENEFIT OF PEOPLE THAT MIGHT NOT HAVE HEARD THIS PRESENTATION BEFORE. SO OUR ANALYSIS AND RECOMMENDATIONS HAVE BEEN GUIDED BY A ROBUST, COMPREHENSIVE DATASET. AND OUR APPROACH HAS BEEN BOTH COMPREHENSIVE AND METICULOUS, ENSURING THAT EVERY STRATEGIC CONSIDERATION IS BACKED BY SOLID DATA AND REAL-WORLD INSIGHTS.

THIS PAGE SHOWS MAIN SOURCES OF DATA THAT WE HAVE CONSULTED INTERNALLY AND EXTERNALLY. SO TO START WITH, WE HAVE THE CALIFORNIA DEPARTMENT OF PUBLIC HEALTH REPORTS, THE CDC, AND THE CANCER REGISTRY REPORTS. THE DATA COLLECTION HERE INCLUDED SEVERAL YEARS LEADING UP TO 2023 AND EARLY 2024 COVERING BOTH PREPANDEMIC AND PANDEMIC PERIODS, WHICH ALLOWED US FOR A COMPREHENSIVE ANALYSIS THAT ACCOUNTS FOR POTENTIAL ABERRATIONS CAUSED BY UNUSUAL EVENTS, SUCH AS COVID-19.

TAKING THIS MULTIYEAR APPROACH HAS HELPED

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

UNDERSTAND BROADER TRENDS IN HEALTH DATA IN CALIFORNIA, ALLOWING US TO ALIGN OUR STRATEGIES WITH THE CURRENT HEALTHCARE LANDSCAPE IN CALIFORNIA.

THEN WE GOT INTO OUR INTERNAL PORTFOLIO DATA ANALYSIS. OF COURSE, FOR THE EARLIER PART, THE GOALS 1 AND 2, WE WERE MORE FOCUSED ON THE DISCOVERY AND EARLY TRANSLATIONAL. TODAY WE ARE GOING TO SEE MORE EVERYTHING, BUT FOCUS ON TRANSLATIONAL, MIDDLE, LATE, AND CLINICAL.

BY EXAMINING OUR HISTORICAL DATA, WE'VE GAINED INSIGHTS INTO THE OUTCOMES AND EFFECTIVENESS OF PAST PROJECTS. AND THAT'S INVALUABLE FOR OUR FUTURE PROJECT SELECTION AND DISTRIBUTION, AND FUNDING DISTRIBUTION.

SO THE NEXT ONE WAS THE INDEPENDENT RESEARCH BY PROJECT LEADS AND SCIENCE OFFICERS. THIS HAS BEEN INVALUABLE. A VERY DEDICATED TEAM OF PROJECT LEADS AND SCIENCE OFFICERS UNDERTOOK A DEEP DIVE INTO THE DIFFERENT ASPECTS OF OUR PORTFOLIO AND LAST DEEP ANALYSIS CAPTURED THROUGH DATABASES AS WELL AS IN PEER REVIEWED PAPERS AND RESEARCH ARTICLES.

THE FOCUS BESIDES PORTFOLIO ANALYSIS WAS ON CELL AND GENE THERAPY AMENABILITY, BIOMARKER NEEDS, STEM CELL MODEL READINESS, AS WELL AS

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

TECHNOLOGY AND BOTTLENECK GAPS.

DURING THE JULY MEETING, WE PRESENTED AND COVERED GOALS 1 AND 2, AND OUR FOCUS WAS A LOT ABOUT THE STEM CELL MODEL READINESS AND THE BIOMARKER NEEDS, TECHNOLOGY AND BOTTLENECKS GAPS. DURING TODAY'S CALL, THIS IS TAKEN INTO ACCOUNT, BUT THE FOCUS HAS BEEN MORE ABOUT CELL AND GENE THERAPY AMENABILITY, THE INDUSTRY LANDSCAPE. AND WE WILL DISCUSS THIS TODAY.

THE NEXT SET OF DATA WAS THE GLOBAL DATABASE, WHICH HAS PROVIDED US WITH A BROADER INDUSTRY PERSPECTIVE. SUCH INFORMATION IS CRITICAL TO ENSURE THAT OUR STRATEGIES ARE NOT ONLY RESPONSIVE TO CURRENT NEEDS, BUT ALSO ANTICIPATORY OF FUTURE SCIENTIFIC AND MARKET SHARES AS WELL.

THEN WE HAVE THE IQVIA CALIFORNIA DISEASE ANALYSIS OF DISEASES AFFECTING THE CALIFORNIA PATIENT POPULATION UTILIZING ANONYMIZED PATIENT CLAIMS DATA FROM OVER 1.5 BILLION PATIENT INTERACTIONS OVER THE PAST YEAR MATCHED TO ICD-10 MEDICAL CODES. THIS ANALYSIS HAS BROUGHT US A DEEP UNDERSTANDING OF DISEASE PREVALENCE AND MANAGEMENT TRENDS ACROSS CALIFORNIA. THIS WAS COMPLEMENTED FROM INSIGHTS FROM SUBJECT MATTER EXPERTS AND HEALTH ECONOMICS DATA TO FURTHER REFINE OUR UNDERSTANDING

OF WHERE STRATEGIC INVESTMENTS CAN BE MOST IMPACTFUL.

WE ALSO GATHERED NIH FUNDING AND INDUSTRY LANDSCAPE DATA.

FINALLY, WE HAD THE NEURO TASK FORCE SURVEY OF 670 NEUROSCIENTISTS ACROSS THE BOARD, WHICH LED TO PRELIMINARY RECOMMENDATIONS THAT HAVE BEEN INCLUDED IN THE OVERALL GOALS AND RECOMMENDATIONS THAT WE'RE PRESENTING TODAY.

TOGETHER, THESE DATA SOURCES CREATE A COMPREHENSIVE PICTURE THAT HAS BEEN GUIDING US AND IS GUIDING US THROUGH OUR STRATEGIC ALLOCATION FRAMEWORK. BUT AN IMPORTANT POINT TO HIGHLIGHT HERE IS THAT THE DATA THAT WE SHOW AT EVERY MEETING IS JUST A SNAPSHOT REPRESENTATIVE OF ALL THE DATA GATHERED THROUGH THESE DATA SOURCES BECAUSE IT'S NOT POSSIBLE TO SHOW ALL THE DATA IN A 2.5 HOUR MEETING. AND THAT'S WHY WE HAVE THE DISCUSSION AS WELL.

A VERY IMPORTANT SLIDE IS TO SHOW WHO HAS BEEN BEHIND THE DATA ANALYSIS AND THE PRESENTATION. DURING THE INITIAL STRATEGIC ALLOCATION FRAMEWORK PRESENTATION THAT WE PROVIDED AN OVERVIEW OF HOW THE LT, THE LEADERSHIP TEAM, AT CIRM HAD BEEN DEVELOPING THE GOALS AND THE QUESTIONS AND DATA NEEDED IN ORDER TO MAKE THE RECOMMENDATIONS. BUT THERE IS ANOTHER

ESSENTIAL GROUP OF PEOPLE WHO HAVE BEEN WORKING VERY HARD OVER THE PAST 3.5 MONTHS GATHERING AND ANALYZING A LOT OF THE DATA, AND THESE PEOPLE ARE LISTED HERE. THERE'S OUR DEDICATED TEAM OF PROJECT LEADS AND SCIENCE OFFICERS THAT HAVE UNDERTAKEN A VERY DEEP DIVE INTO THE DIFFERENT ASPECTS OF OUR PORTFOLIO AND LANDSCAPE ANALYSIS THAT HAS BEEN CAPTURED THROUGH THE DATABASES THAT I MENTIONED, AS WELL AS PEER REVIEWED PAPERS AND ARTICLES BECAUSE SOME OF THE DATA CANNOT BE EXTRACTED THROUGH DATABASE. YOU HAVE TO GO INTO DEEP DIVE OF LITERATURE REVIEWS.

I WOULD LIKE TO ACKNOWLEDGE THREE SPECIAL PEOPLE HERE: DR. SARA TAYLOR, THOMAS TRINH. WITHOUT THE COORDINATION OF TEAM MEMBERS AND THE ANALYSIS OF PUTTING TOGETHER THIS PRESENTATION, THIS COULD NOT HAVE BEEN POSSIBLE WITHOUT THEM. AND ALSO DR. SHYAM PATEL, WHO BESIDES BEING A MEMBER OF THE LEADERSHIP TEAM, HE LED AND COORDINATED THE GLOBALDATA AND IQVIA EXTERNAL ANALYSIS EFFORTS AND COORDINATING SCIENCE OFFICER ANALYSIS AMONGST MANY OTHER THINGS. SO ALL OF THESE CONTRIBUTIONS WERE MADE IN CONJUNCTION WITH THEIR REGULAR DUTIES, UNDERSCORING THE DEDICATION OF OUR TEAM. AND WE ARE PROFOUNDLY GRATEFUL FOR THEIR COMMITMENT AND

EXCELLENCE.

SO NOW WE ARE GOING TO GO INTO THE DATA. AND BEFORE WE MOVE INTO THAT, WE ARE GOING TO HAVE A QUICK REFRESH, RECAP OF OUR RESEARCH AND DEVELOPMENT PIPELINE OF PROGRAMS, WHICH ENCOMPASS THE FULL SPECTRUM OF RESEARCH AND DEVELOPMENT FROM THE EARLIER STAGES OF DISCOVERY THROUGH TO CLINICAL DEVELOPMENT.

SO THE FIRST PART IS FOR THE EARLIER PART OF OUR DISCOVERY PROGRAMS. WHAT I WANT TO MENTION IS IND DISCOVERY 0, DISC4, DISC5 ARE NOT INCLUDED HERE. THAT'S FOUNDATIONAL RESEARCH. DISC2 IS ACTUALLY CONSIDERED EARLY TRANSLATION. SO OUR EARLY TRANSLATIONAL PROGRAM THROUGH DISC2 OFFERS AN EARLY TRANSLATIONAL PROGRAM THAT SUPPORTS ACTIVITIES THAT WILL LEAD TO THE SELECTION OF A NOVEL THERAPEUTIC CANDIDATE OR BIOMARKER. THIS IS NEW. THAT'S WHY DISC4 TRANSLATION. AND THE EXPECTED OUTCOME OF THESE TWO AWARDS IS TO PRODUCE A PROJECT DELIVERABLE THAT CAN IMMEDIATELY PROGRESS TO TRANSLATIONAL ACTIVITIES.

AND THE NEXT STEP IN OUR PIPELINE, CIRM OFFERS CURRENTLY THREE TRANSLATIONAL TYPES OF OPPORTUNITIES, THAT THEY FOCUS ON PRECLINICAL STAGE ACTIVITIES TO POSITION EITHER THROUGH TRAN1 COULD BE

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

A THERAPEUTIC CANDIDATE FOR THE INITIATION OF IND-ENABLING PRECLINICAL STUDIES FOR IND FILING WITH THE FDA IN THE DEVELOPMENT OF STEM CELL, GENETIC RESEARCH, OR COMBINATION, OR BIOLOGICAL SMALL MOLECULE. THEN TRAN2 FOCUSES ON DIAGNOSTICS, MIDDLE TRANSLATIONAL EXERCISE, AND THEN TRAN4, NOVEL TOOLS FOR BROAD USE, ADDRESSING CRITICAL BOTTLENECKS TO THE DISCOVERY OR DEVELOPMENT OF STEM CELL AND GENE THERAPIES. SO THAT'S TRAN RIGHT NOW IN A NUTSHELL.

NOW WE HAVE THE CLINICAL PORTFOLIO. SO THE CLINICAL PORTFOLIO CURRENTLY INCLUDES THREE PROGRAMS. CLIN1 IS ACTUALLY CONDUCTING -- SUPPORTS PROJECTS CONDUCTING LATE-STAGE TRANSLATIONAL RESEARCH, CORRESPONDING TO IND-ENABLING STUDIES. CLIN2 AWARDS FOR CLINICAL TRIALS, POST-IND FILING, AND FDA PROTOCOL CLEARANCE, EITHER A PHASE 1 OR 2, DEPENDING ON WHERE THE COME IN, RECEIVE DIFFERENT AMOUNTS OF FUNDING, BUT THAT'S ALREADY CLINICAL TRIALS PHASE 1 AND 2. AND THEN CLIN4, WHICH IS OUR NEWEST PROGRAM FOR AWARDS, TO SUPPORT ACTIVE CLIN2 PROJECTS, AIMING FOR MARKETING APPROVAL, READINESS, AND PRECOMMERCIAL ACTIVITIES.

SO THROUGH THESE THREE PILLARS, CIRM FUNDS THE ENTIRE SPECTRUM OF RESEARCH FROM EARLIER TRANSLATION THROUGH TO CLINICAL DEVELOPMENT.

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

NOW, BASED ON THAT KNOWLEDGE, HOW MUCH OF OUR HISTORICAL PORTFOLIO IS RARE VERSUS ULTRA-RARE DISEASES? AND THIS INFORMATION IS DATA ANALYSIS GOALS 3 AND 4, CORRESPONDING FOR GOALS 3 AND 4.

SO THE DATA ON CIRM'S HISTORICAL PORTFOLIO, AND THE NEXT SLIDE IS GOING TO BE ABOUT ACTIVE PORTFOLIO, BUT RIGHT NOW IS HISTORICAL -- REVEALS A NOTABLE TREND AT THE DISCOVERY AND TRANSLATIONAL STAGES. THERE IS A SLIGHT MAJORITY FOCUS ON PREVALENT DISEASES WITH THE DISTRIBUTION BEING APPROXIMATELY 55 PERCENT PREVALENT VERSUS 45 PERCENT RARE AND ULTRA-RARE.

AS WE MOVE INTO THE LATER STAGES OF DEVELOPMENT, PARTICULARLY THE IND-ENABLING, CLIN1, AND POST-IND, CLIN2 ACTIVITIES, THIS TREND SHIFTS. AND THE FOCUS STILL IS TOWARDS RARE AND ULTRA-RARE DISEASES WITH THE DISTRIBUTION REVERSING TO APPROXIMATELY 45 PERCENT PREVALENT VERSUS 55 RARE AND ULTRA-RARE. THIS SHIFT UNDERSCORES CIRM'S STRATEGIC EMPHASIS ON ADVANCING THERAPIES FOR RARE AND ULTRA-RARE DISEASES AS THEY PROGRESS CLOSER TO CLINICAL APPLICATION AND POTENTIAL MARKET APPROVAL.

NOW, FOR THE CURRENT ACTIVE PORTFOLIO, THE TRENDS MENTIONED ARE MAINTAINED IN OUR ACTIVE PORTFOLIO IS ABOUT THE SAME TREND. LARGER

PROPORTION OF THE PREVALENT ARE FOR DISC AND TRAN; WHEREAS, THERE IS A SHIFT WITH 54 PERCENT OF CLIN FUNDING CORRESPONDING TO RARE AND ULTRA-RARE DISEASES.

THIS SLIDE PRESENTS A DETAILED OVERVIEW OF THE LANDSCAPE OF CELL AND GENE THERAPY ACROSS A SPECTRUM OF DISEASES, AND THE FOCUS ON THOSE THAT ARE SIGNIFICANTLY IMPACTING THE CALIFORNIA POPULATION. TO GIVE AN OVERVIEW OF DISEASES AFFECTING CALIFORNIANS, WE FOCUSED ON 16 DISEASES. SO THERE ARE TWO SLIDES. THE SECOND SLIDE SHOWS THE CANCERS THAT AFFECT MOST CALIFORNIANS. WE FOCUSED ON THESE 16 DISEASES THAT ARE KNOWN TO AFFECT MOST CALIFORNIANS.

AND WHAT WE OBSERVED IS THAT WHILE THERE IS A SIGNIFICANT ACTIVITY IN CELL AND GENE THERAPY PIPELINE AS INDICATED IN THE COLUMN BY THE GLOBAL CGT PIPELINE WITH MANY CANDIDATES ACROSS A RANGE OF DISEASES. THE MAJORITY OF THESE ARE STILL IN PRECLINICAL OR EARLY CLINICAL STAGES.

AS WE ALL KNOW, CIRM HAS YET TO FUND ANY PROJECT THAT HAS SUCCESSFULLY LED TO AND APPROVAL THERAPY ALTHOUGH WE HAVE, AS I MENTIONED EARLIER ON, A PIPELINE OF PROJECTS OR PROGRAMS THAT ARE LEADING IN THE NEXT TWO TO FOUR YEARS TO BLA APPROVAL. AND

WE HAVE A HUNDRED -- ABLA WILL HAVE TO TELL ME -- 14, I THINK IT IS, CLINICAL TRIALS. BUT THIS REFLECTS THE BROADER REALITY OF THE FIELD. MOST CELL AND GENE THERAPY EFFORTS ARE STILL IN THE EARLY STAGES AND HAVE NOT YET REACHED COMMERCIALIZATION. THERE ARE A FEW EXCEPTIONS WITH APPROVALS PRIMARILY SEEN IN, AS YOU CAN SEE, THE TYPE 1 DIABETES AND, AS YOU WILL SEE IN THE NEXT TWO SLIDES, IN THE NEXT SLIDE, FOR TWO CANCERS, MELANOMA AND PROSTATE CANCER HAVE A CELL OR GENE THERAPY APPROVAL IN THE U.S. MARKET.

THIS UNDERSCORES THE ONGOING CHALLENGES AND THE LONG DEVELOPMENT TIMELINE ASSOCIATED WITH BRINGING THESE INNOVATIVE THERAPIES TO MARKET AND RELEVANT TO THIS STRATEGIC EXERCISE LEADING TO RECOMMENDATIONS TO MAXIMIZE THE IMPACT AND EXPEDITED DEVELOPMENT OF THESE PROMISING THERAPIES IN THE CELL AND GENE THERAPY DOMAIN.

AND THIS IS THE SLIDE, CONTINUATION OF THE PREVIOUS SLIDE, SHOWING THE FIVE CANCERS THAT AFFECT MOST CALIFORNIANS WITH THE PATIENT COUNT AND THE ECONOMIC BURDEN AS WELL AS THE GLOBAL CGT PIPELINE CARED AS A REFERENCE TO STROKE, WHICH AS YOU CAN SEE COMPARED TO BEFORE STROKE WAS RIGHT HERE. AND IT'S JUST TO GIVE A REFERENCE OF HOW MANY PATIENTS ARE

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

AFFECTED BY THE MOST -- THE CANCERS THAT AFFECT MOST CALIFORNIANS. AND, AGAIN, THIS UNDERSCORES THE ONGOING CHALLENGES IN THE LONG DEVELOPMENT TIMELINES ASSOCIATED WITH BRINGING THESE THERAPIES TO APPROVAL.

SO AS A FOLLOW-UP FROM THIS ANALYSIS, OUR TEAM ENGAGED IN AN IN-DEPTH ANALYSIS OF THE FIELD AND OUR PORTFOLIO TO FIGURE OUT WHERE ARE THE MAIN CHALLENGES THAT ARE PRECLUDING THESE THERAPIES FROM MOVING THROUGH THE PIPELINE AND ESPECIALLY FOCUSING ON OUR PORTFOLIO, BUT ALSO HAVING INTO ACCOUNT LIKE HOW THIS REFLECTS THE EXTERNAL LANDSCAPE AND WHICH OPPORTUNITIES CAN HELP US MOVE THE PORTFOLIO TOWARDS APPROVALS.

SO THE NEXT SLIDE IS A SUMMARY OF THIS AND WILL HELP IN THINKING ABOUT HOW WE PLANNED THE RECOMMENDATIONS IS WE HAVE MAPPED THE RECOMMENDATIONS TO THESE CHALLENGES AND OPPORTUNITIES. AND I'LL TRY TO GO STEP BY STEP THERE.

SO OUR FIRST OPPORTUNITY IS THE FRAMEWORK ESTABLISHED BY PROP 14 WHICH MANDATES SUPPORT FOR THERAPIES THAT BENEFIT CALIFORNIANS. THEN WE FOCUSED ON CHALLENGES IN THE RESEARCH AND DEVELOPMENT PIPELINE. AND AT THE LEVEL OF

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

TRANSLATIONAL GAPS AND OPPORTUNITIES, THERE IS A SIGNIFICANT CHALLENGE IN OUR PIPELINE, WHICH IS THE DISCONNECT BETWEEN THE EARLY AND LATE TRANSLATIONAL PHASES. WE NEED TO BRIDGE THIS GAP AND BETTER ALIGN THE PROGRAMS TO ENSURE THAT PROMISING DISCOVERIES CAN MOVE EFFICIENTLY FROM EARLY STAGES TO THE CLINICAL DEVELOPMENT.

ADDITIONALLY, AS THE FIELD MATURES, THERE ARE OPPORTUNITIES TO STREAMLINE THESE PROCESSES OF REDUCING TIME AND COST ACCELERATE THIS TRANSITION TO CLINICAL TRIALS.

ANOTHER CHALLENGE IS DEVELOPMENT COMPLEXITIES FOR RARE DISEASES. DEVELOPING GENE THERAPIES IS INTEGRALLY COSTLY AND TIME-CONSUMING, MAKING IT PARTICULARLY CHALLENGING TO SCALE THESE EFFORTS ACROSS THE THOUSANDS OF RARE DISEASES THAT EXIST. AND THIS COMPLEXITY HIGHLIGHTS THE NEED FOR INNOVATIVE APPROACHES TO MAKE THESE THERAPIES MORE ACCESSIBLE TO A BROADER RANGE OF RARE CONDITIONS.

THE REGULATORY AND LATE-STAGE CHALLENGES ARE REFLECTED HERE. AS WE MOVE INTO CLINICAL PHASES, REGULATORY INNOVATION PRESENTS AN OPPORTUNITY TO ENHANCE THE EFFICIENCY OF CLINICAL STUDIES. AND THIS CAN BE ACHIEVED THROUGH MASTER PROTOCOLS THAT ALLOW THE SIMULTANEOUS EVALUATION OF

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

MULTIPLE THERAPIES FOR DIFFERENT DISEASES, POTENTIALLY SPEEDING THE DEVELOPMENT PROCESS.

APPROVED CELL AND GENE THERAPIES OFTEN FACE ALSO PATIENT ACCESS CHALLENGES. SO INCENTIVIZING STAGE-APPROPRIATE MARKET ACCESS STRATEGY DEVELOPMENT AND PRECOMMERCIALIZATION ACTIVITIES IN THE APPROPRIATE PROGRAMS COULD INCREASE THE PROBABILITY OF PATIENT ACCESS TO THERAPIES.

MOREOVER, LATE-STAGE PROGRAMS OFTEN REQUIRE EXTENSIVE INVESTMENT, PARTICULARLY IN CMC. THESE REQUIREMENTS CAN DELAY READINESS OF BIOLOGICAL LICENSE APPLICATION FILINGS. AND THIS UNDERSCORES THE NEED FOR STRATEGIC PLANNING AND RESOURCE ALLOCATION IN THE LATER STAGES OF DEVELOPMENT. THIS IS A NEW PROGRAM THAT WE HAVE, AND WE'VE COVERED FEEDBACK, AND WE ARE ADDRESSING THESE CHALLENGES TO MOVE THIS FORWARD.

SO WE ARE ADDRESSING THESE THROUGH BOTH GOALS. ALL THESE CHALLENGES AND OPPORTUNITIES ARE BEING ADDRESSED THROUGH THE RECOMMENDATIONS OF BOTH GOALS 3 AND 4 THAT WE WILL PRESENT IN THE NEXT SLIDES. SO THOSE ARE GOALS 3 AND 4.

GOAL 3, AS A REMINDER, FOCUSES ON ADVANCING AT LEAST X-RARE DISEASE PROJECTS TO BLA

READINESS. ACHIEVING THIS GOAL REQUIRES ADDRESSING KEY BOTTLENECKS IN THE PIPELINE AND IMPLEMENTING STRATEGIC INITIATIVES TO ENHANCE THE EFFICIENCY AND SCALABILITY OF GENE THERAPY DEVELOPMENT FOR RARE DISEASES.

HOW? THROUGH OUR RECOMMENDATIONS. SO AS I MENTIONED, ONE SIGNIFICANT BOTTLENECK IN THE ADVANCEMENT OF RARE-DISEASE THERAPIES IS THE EXTENSIVE INVESTMENT REQUIRED FOR LATE-STAGE PROGRAMS, PARTICULARLY CHEMISTRY, MANUFACTURING, AND CONTROLS, CMC. THESE CHALLENGES OFTEN PREVENT OR DELAY BLA READINESS, HINDERING THE PROGRESSION OF PROMISING THERAPIES.

SO OUR RECOMMENDATION TO OVERCOME THESE CHALLENGES IS TO INCREASE AND SCALE CLIN4 FUNDING. THIS FUNDING WILL COMPREHENSIVELY ADDRESS BLA READINESS GAPS IN MANUFACTURING, CLINICAL AND NONCLINICAL RESEARCH, AND PRECOMMERCIALIZATION ACTIVITIES. AND BY DOING SO, WE CAN INCREASE THE SPEED AND PROBABILITY OF SUCCESS FOR BLA SUBMISSIONS, ULTIMATELY ACCELERATING THE AVAILABILITY OF THERAPIES TO PATIENTS IN NEED.

THE SECOND CHALLENGE AND RECOMMENDATION, THE CHALLENGE IN THE DEVELOPMENT OF GENE THERAPIES IS INHERENTLY COSTLY AND TIME-CONSUMING, POSING A

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

SIGNIFICANT CHALLENGE ESPECIALLY WHEN SCALING ACROSS THOUSANDS OF RARE DISEASES. AND THE TRADITIONAL APPROACH TO DEVELOP THERAPIES ON A CASE-BY-CASE BASIS IS NOT SUSTAINABLE GIVEN THE DIVERSITY AND NUMBER OF RARE DISEASES.

SO OUR RECOMMENDATION, AND THIS IS NOT NEW TO THE BOARD, THERE HAS BEEN A LOT OF WORK AROUND THIS, TO ADDRESS THIS ISSUE, WE RECOMMEND IMPLEMENTING A PILOT PLATFORM-BASED APPROACH FOR GENE THERAPY DEVELOPMENT. THIS APPROACH WILL FOCUS ON LIFE-THREATENING, MONOGENIC NEUROLOGICAL DISORDERS AS A TEST CASE. AND BY USING A PLATFORM-BASED MODEL, WE AIM TO DEMONSTRATE THAT THIS METHOD CAN ENABLE THE RAPID, SUSTAINABLE, AND SCALABLE DEVELOPMENT OF GENE THERAPIES THAT CAN BE APPLIED TO MULTIPLE RARE DISEASES.

DR. ABLA CREASEY HAS BEEN LEADING THIS ENDEAVOR AND HAS ALREADY BEEN WORKING ON THIS AND ENGAGED FDA AND OTHER FEDERAL AND INDUSTRY STAKEHOLDER LEADERS, WHICH GIVES US, AS WELL AS THE WORKSHOP THAT WAS CARRIED OUT LATE 2023, AND THIS GIVES US CONFIDENCE THAT THIS IS JUST NOT -- THIS IS NOT JUST AN ASPIRATIONAL GOAL, BUT IS SOMETHING THAT WE'VE BEEN THINKING A LOT. AND IF APPROVED, THE RECOMMENDATION COULD TAKE FORM OF A CONCEPT FOR

BOARD CONSIDERATION BETWEEN SEPTEMBER AND DECEMBER OF THIS YEAR.

SO THIS IS JUST TO SHOW THE BOTTLENECKS THAT WE JUST COVERED. GOAL 4 IS FOCUSED ON PROPELLING THERAPIES TARGETING DISEASES AFFECTING CALIFORNIANS TO LATE-STAGE CLINICAL TRIALS. AND TO ACHIEVE THIS, WE NEED TO ADDRESS SEVERAL BOTTLENECKS AND LEVERAGE OPPORTUNITIES WITHIN OUR PRECLINICAL AND CLINICAL DEVELOPMENT PROGRAMS.

THE RECOMMENDATIONS OUTLINED HERE AIM TO STREAMLINE THE DEVELOPMENT PROCESS, PRIORITIZE THERAPIES THAT BENEFIT CALIFORNIANS, AND ADDRESS CHALLENGES IN REGULATORY INNOVATION AND PATIENT ACCESS.

SO THE FIRST ONE IS TO STREAMLINE PRECLINICAL DEVELOPMENT PROGRAMS. THERE IS AN OPPORTUNITY. CURRENTLY OUR TRANSLATIONAL PIPELINE, WHICH INCLUDES FIVE PROGRAMS, THE DISC2, TRAN1, 2, 3 AND CLIN1, IS AT TIMES DISCONNECTED AND REDUNDANT, WHICH CREATES DELAYS IN ADVANCING THERAPIES TO THE CLINICAL STAGE. AS THE FIELD OF CELL AND GENE THERAPY MATURES, THERE'S AN OPPORTUNITY TO STREAMLINE THIS PRECLINICAL DEVELOPMENT, ALSO TO ALIGN IT WITH THE INFRASTRUCTURE TECHNOLOGY PLATFORM THAT WE TALKED ABOUT IN GOAL 2, AND OUR

MANUFACTURING AS WELL.

SO TO ADDRESS THESE, WE RECOMMEND CONSOLIDATING DISC2, TRAN1, 2, AND 4 AND CLIN1 TOWARD ACCELERATING PRECLINICAL DEVELOPMENT, INCENTIVIZING MULTIDISCIPLINARY COLLABORATIONS, AND FOSTERING RAPID PROGRESSION TO IND. WE DON'T MEAN THAT IT WILL BE JUST ONE PROGRAM, BUT WE ARE MEANING TO COMBINE AND MAKE IT MORE STREAMLINED. WE WOULD INCREASE -- THE POTENTIAL OUTCOME HERE WOULD BE THAT WE WOULD INCREASE THE PROBABILITY OF PROPELLING THERAPIES MORE EFFICIENTLY INTO LATE-STAGE CLINICAL TRIALS.

THE SECOND RECOMMENDATION IS TO PRIORITIZE INNOVATIVE THERAPIES FOR CALIFORNIANS. AND THIS HAS TO DO WITH THE PRIORITY AND OPPORTUNITY FROM PROPOSITION 14 MANDATE, THAT CIRM SUPPORTS THERAPIES FOR DISEASES AFFECTING CALIFORNIANS. WE THINK THAT IT IS ESSENTIAL THAT OUR FUNDING PRIORITIZATION PROCESSES REFLECT THIS EXPECTATION. AND WE PROPOSE INCORPORATING A PRIORITIZATION MECHANISM WITHIN OUR TRANSLATIONAL AND CLINICAL PROGRAMS THAT EMPHASIZES INNOVATIVE THERAPIES TARGETING DISEASES WITH CLINICAL IMPACT ON -- WITH SIGNIFICANT, NOT CLINICAL, WITH SIGNIFICANT IMPACT TO CALIFORNIANS.

THE NEXT SET OF RECOMMENDATIONS HAVE TO DO

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

WITH AN UPDATE -- CORRESPOND TO UPDATES IN THE CLIN2 PROGRAM. THERE IS AN OPPORTUNITY FROM THE REGULATORY FIELD. REGULATORY INNOVATION OFFERS A PATHWAY TO ENABLE CLINICAL STUDIES OF MULTIPLE THERAPIES ACROSS MULTIPLE DISEASES THROUGH MASTER PROTOCOLS. AND THIS CAN GREATLY ENHANCE THE EFFICIENCY OF CLINICAL TRIALS. AND WE RECOMMEND UPDATING THE CLIN2 PROGRAM TO SUPPORT EMERGING NOVEL CLINICAL TRIAL DESIGNS, WHICH COULD INCLUDE ADOPTION OF MASTER PROTOCOLS THAT COULD ALLOW FOR SIMULTANEOUS EVALUATION OF MULTIPLE THERAPIES.

THE POTENTIAL OUTCOME HERE WOULD BE THAT BY EMBRACING INNOVATIVE TRIAL DESIGNS, WE INCREASE THE PROBABILITY OF PROPELLING THERAPIES TO LATE-STAGE CLINICAL TRIALS AND INCLUDING OVERALL EFFICIENCY OF THE DEVELOPMENT PIPELINE.

THE SECOND RECOMMENDATION IS TO ENHANCE PATIENT ACCESS THROUGH MARKET STRATEGY AND PRECOMMERCIALIZATION. EVEN WHEN THERAPIES ARE APPROVED, THEY OFTEN FACE SIGNIFICANT CHALLENGES IN TERMS OF PATIENT ACCESS, PARTICULARLY DUE TO GAPS IN MARKET ACCESS STRATEGIES AND PRECOMMERCIALIZATION PLANNING.

THE SOLUTION THAT WE PROPOSE HERE IS TO MITIGATE THIS, THAT THE CLIN2 PROGRAM SHOULD

INCENTIVIZE STAGE-APPROPRIATE MARKET ACCESS STRATEGY DEVELOPMENT AND PRECOMMERCIALIZATION ACTIVITIES TO ENSURE THAT, AS THERAPIES ADVANCE, THEY ARE ALSO PREPARED FOR SUCCESSFUL MARKET ENTRY AND PATIENT ACCESS.

THIS SLIDE IS A SUMMARY OF WHAT WE JUST PROPOSED. BY STREAMLINING PRECLINICAL PROGRAMS, PRIORITIZING THERAPIES FOR CALIFORNIANS, EMBRACING INNOVATIVE CLINICAL TRIAL DESIGNS, AND ENHANCING MARKET ACCESS STRATEGIES, WE CAN OVERCOME SOME OF THE EXISTING BOTTLENECKS AND SEIZE OPPORTUNITIES TO PROPEL PROMISING THERAPIES TO LATE-STAGE TRIALS AND ULTIMATELY TO PATIENTS WHO NEED THEM.

AND THE NEXT SLIDE IS A SUMMARY. WE'RE GETTING THERE, 40 MINUTES PRESENTATION. THE PROPOSED CHANGES TO PROGRAMS. ON THE LEFT YOU HAVE THE CURRENT PROGRAMS AS THEY ARE AND ON THE RIGHT HOW THE RECOMMENDATIONS FOR GOALS 3 AND 4 COULD AFFECT OR COULD CHANGE THE CURRENT PROGRAMS.

SO CLIN2 AND 4 PROGRAMS, WE ARE CURRENTLY PREVALENT, RARE, AND ULTRA-RARE DISEASES ARE ELIGIBLE FOR THE SAME FUNDING OPPORTUNITIES. AND WE WOULD BE PRIORITIZING INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT CALIFORNIANS. WE COULD ALSO PILOT A RARE-DISEASE PLATFORM PROGRAM WITH A FOCUS

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

ON RARE AND ULTRA-RARE DISEASES AND REQUIREMENT FOR ACADEMIC/INDUSTRY LEADER PARTNERSHIPS.

THE CLIN2 SUPPORTS INDIVIDUAL CLINICAL TRIALS FOR SINGLE CANDIDATES AND SUPPORTS A SUBSET OF PRECOMMERCIALIZATION ACTIVITIES. AND WITH THE RECOMMENDATIONS, WE COULD SUGGEST TO SUPPORT INNOVATIVE CLINICAL TRIAL DESIGN AND INCENTIVIZING MARKET ACCESS STRATEGY DEVELOPMENT AND PRECOMMERCIALIZATION ACTIVITIES.

FOR CLIN4, THE FUNDING IS INSUFFICIENT FOR ALL ACTIVITIES NEEDED TO REACH BLA READINESS. THIS COMES FROM FEEDBACK AND EXPERIENCE WITH THE FIRST SET OF AWARDEES. SO CLIN4 FUNDING WE RECOMMEND TO INCREASE AND SCALE TO COMPREHENSIVELY ADDRESS BLA READINESS GAPS.

IN TERMS OF THE MULTI-PROGRAM PRECLINICAL PATH, WE HAVE CURRENTLY SEPARATED DISC2, TRAN1, 2, 4, CLIN1 PROGRAMS WITH THEIR OWN APPLICATIONS THAT, AS WE MENTIONED, HAVE A DISCONNECT AND ARE AT TIMES REDUNDANT. AND PREVALENT, RARE, AND ULTRA-RARE DISEASES ARE ELIGIBLE FOR THE SAME FUNDING OPPORTUNITIES. WE COULD PROPOSE A CONSOLIDATED PRECLINICAL PROGRAM. AND THE DETAILS OF THAT COULD COME THROUGH A CONCEPT OR TWO. AND PRIORITIZE INNOVATIVE THERAPIES FOR DISEASES THAT AFFECT

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

CALIFORNIANS AGAIN.

WE'RE GOING TO GO THROUGH THE DISCUSSION AND NEXT STEPS NOW. LET ME SEE IF I HAVE -- SO I CAN GO -- WELL, WE CAN GO TO THE NEXT STEPS AT THE END, MARK, IF YOU WANT. THE NEXT STEPS IS BASICALLY TALKING ABOUT THIS AND THIS, BUT PERHAPS WE GO THROUGH THE DISCUSSION NOW. WHAT WOULD YOU LIKE TO DO?

CHAIRMAN FISCHER-COLBRIE: YES. LET'S GO THROUGH THE DISCUSSION. AND THE TIMELINES ARE EXTREMELY RELEVANT TO THE FACT THAT THIS IS AN ONGOING PROCESS. AND J.T. IS LIKELY TO HAVE ADDITIONAL COMMENTS AROUND THIS. BUT AS FROM A SUPER TOP LEVEL, NOT ONLY ARE WE ATTEMPTING TO ENSURE WE'RE IN FULL ALIGNMENT WITH THE MISSION OF CIRM, WHICH HAS TO DO WITH TRANSFORMATIONAL WORK, INCLUDING WORK NOT DONE BY OTHER ORGANIZATIONS, AS WELL AS THE ABILITY TO HAVE A BROAD-SCALE IMPACT ALONG WITH CREATION OF LEVERAGE. SO ELEMENTS AROUND PROTOCOLS THAT WOULD INDICATE MULTIPLE DISEASE OPPORTUNITIES, STREAMLINING OUR OWN INTERNAL PROCESSES FOR APPROVAL, RESOLVING GAPS IN CONTINUITY, ALL THESE THINGS HAVE DIRECT EXPOSURE TO THAT.

AND WITHIN THE OVERALL PROCESS CONTEXT,

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

NOT ONLY HAS THERE BEEN A MASSIVE AMOUNT OF WORK DONE, BUT THIS IS A SITUATION WHERE WE NEED YOUR DIRECT INVOLVEMENT HERE AND DIRECT FEEDBACK BECAUSE OF THE FACT THAT IT'S SO ESSENTIAL THAT WE DO THE BEST JOB WE CAN IN ORDER TO PREPARE SOMETHING FOR CONSIDERATION BY THE BOARD WHICH IS ALSO A PROCESS FOR ASSESSMENT AND EVALUATION.

SO WE NEED YOUR COLLECTIVE WISDOM TO DIVE IN ON THIS. AND NOW IS THE TIME TO COMMENT AND REVIEW. YOU'RE GOING TO NEED LIKELY SOME TIME TO DIGEST THIS A LITTLE BIT. SO FOLLOW-ON COMMENT AND REVIEW IS MORE THAN ACCEPTED, BUT THE IDEA, THEN, IS TO THEN HAVE A FURTHER DIALOGUE AS WE GO FORWARD INTO SEPTEMBER WITH THE BOARD. AND AGAIN, THOSE ARE DIALOGUES. THAT IS NOT, HEY, THE STAFF IS PRESENTING A PLAN IN CONCRETE THAT IS NOT TO BE GAINSAID IN TERMS OF DISCUSSION. SO I THINK THAT GOES WITHOUT SAYING, BUT I JUST WANTED TO ARTICULATE THAT JUST FOR AVOIDING SOME DOUBT.

SO, J.T., I DON'T KNOW IF YOU WANT TO AMPLIFY THAT OR ANY OTHER COMMENTS YOU MIGHT HAVE.

DR. THOMAS: NO. I THINK THAT'S VERY WELL SAID. THIS IS MEANT ALL ALONG TO BE A TEAM EFFORT BETWEEN THE MEMBERS OF THE INTERNAL TEAM AND THE BOARD. AND SO NOTHING WHATSOEVER IS CAST IN STONE.

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

THESE ARE I SAY MERELY A SET OF GOALS AND RECOMMENDATIONS THAT MERELY WOULD SUGGEST NOT A LOT WENT INTO IT, WHICH, OF COURSE, IS CERTAINLY COULDN'T BE FURTHER FROM THE TRUTH. BUT THIS IS SOMETHING THAT WE WANT EVERYBODY'S INPUT ON HERE AND AT THE BOARD SO THAT WE'RE AS INFORMED AS WE CAN BE WHEN WE GET TO THE DECISION-MAKING PROCESS THAT WILL HAPPEN AT THAT MEETING. SO I'LL LEAVE IT AT THAT, MARK. THANK YOU.

CHAIRMAN FISCHER-COLBRIE: GREAT. JUST ONE OTHER COMMENT. I AM BEYOND IMPRESSED WITH NOT JUST THE MASSIVE HOURS THAT HAVE GONE INTO THIS, BUT ALSO THE HYPER QUALITY OF THE WORK. IN FACT, I'M CONVINCED SOME OF THIS CAN BE WRITTEN UP FOR OTHER ORGANIZATIONS TO FOLLOW IN THE FUTURE. THAT'S HOW SEMINAL I THINK WHAT THE TEAM HAS EFFECTIVELY ACCOMPLISHED. BUT I'M ALSO IMPRESSED BY THE BROAD SCALE TEAMWORK WITHIN THE ORGANIZATION. AND WE'RE ALL PART OF THAT TEAM. SO IT'S EXTREMELY IMPORTANT THAT WE PROVIDE OUR FEEDBACK BOTH TODAY AND IN THE COMING WEEKS AS WE GO FORWARD.

AND WITH THAT, I'D LIKE, CAROLYN, IF YOU HAVE SOME COMMENTS.

DR. MELTZER: YEAH. THANKS SO MUCH, MARK. I ALSO WANTED TO ECHO THAT THIS WAS AN INCREDIBLE

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

AMOUNT OF WORK AND CAREFUL ANALYSIS FROM ROSA AND THE TEAM.

I'M WONDERING IF IT WOULD -- IT'S SO MUCH THAT WAS PRESENTED. I'M WONDERING IF IT MIGHT BE HELPFUL TO GO TO THE HIGH-LEVEL QUESTIONS THAT THE DATA SUPPORTED TO HAVE THE BOARD HAVE A LITTLE BIT OF INPUT INTO. QUESTIONS AROUND RARE DISEASE, PREVALENT DISEASES, HOW WE WOULD ADDRESS SOME OF THE MORE CHALLENGING HURDLES, WHETHER IT WOULD BE CONSORTIUM GRANTS, THE PARTNERSHIPS WITH INDUSTRY, ALL OF THE RICH IDEAS THAT WERE PRESENTED, BUT MAYBE GET SOME FEEDBACK ON THOSE. JUST A SUGGESTION ON HOW WE MIGHT PROCEED.

CHAIRMAN FISCHER-COLBRIE: OKAY. SHOULD WE JUST JUMP INTO THAT? WOULD THAT BE THE RIGHT APPROACH?

DR. MELTZER: I THINK MONICA ALSO HAD A COMMENT.

CHAIRMAN FISCHER-COLBRIE: MONICA, YOU'VE GOT SOME COMMENTS HERE?

DR. CARSON: JUST HAVE TO ECHO. THIS IS SUCH AN IMPRESSIVE THING, AND I HAVE TO SAY THE COMMENT THAT THIS WHOLE PROCESS SHOULD BE PUBLISHED SHOULD ACTUALLY BE TAKEN QUITE SERIOUSLY. THIS IS SUCH A BIG THING AND A PROCESS. SO I REALLY WOULD

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

JUST LIKE TO DOUBLE-DOWN ON THAT.

I AM SURE THIS HAS BEEN CONSIDERED IN THE MAGNITUDE OF DATA THAT YOU HAVE PRESENTED. YOU CAN'T PRESENT EVERYTHING. BUT JUST SORT OF TO GET IT ON THE RECORD KIND OF THING, THAT YOU HAVE THOUGHT ABOUT THESE THINGS, WHEN WE TALK ABOUT ALL CALIFORNIANS, CALIFORNIA, WE'RE NOT A HOMOGENEOUS STATE. WE'RE A HIGHLY HETEROGENEOUS STATE REGIONALLY, SOCIOECONOMIC DEMOGRAPHICS, VARIOUS RACIAL ETHNICITIES, GROUPS, AND ALL OF THAT. AND THE HEALTH DISPARITIES, INEQUITIES BETWEEN THOSE ARE GREAT. AND THEN, LASTLY, WHEN WE'RE CONSIDERING THINGS, IN MY FIELD WHEN WE'RE LOOKING AT GWAS DATABASE'S PATIENT CLAIMS, THEY ARE NOT EVENLY DISTRIBUTED AROUND THE REAL INCIDENCE OF DISEASES AND HOW THEY'RE RECORDED.

YOU CAN'T DO ALL THE ANTHROPOLOGY, SOCIOLOGY, AND MEDICAL ANTHROPOLOGY, BUT I KNOW THAT YOU HAVE OFTEN BEEN VERY CONSIDERED, THIS MAY NOT BE THE TIME TO PUT IT UP, BUT I THINK THAT SHOULD ALSO BE PART OF THE RECORD AND THE CONSIDERATIONS OF HOW THESE THINGS ARE PRIORITIZED AND ALSO UNDERSTANDING THE CHALLENGES OF MAKING IMPACT ON SOME OF THESE THINGS AS WELL. THANK YOU.

CHAIRMAN FISCHER-COLBRIE: AND THEN BEFORE

I LAUNCH INTO SOME OF THE FOLLOW-UP ELEMENTS, MARIA, DO YOU HAVE COMMENT?

VICE CHAIR BONNEVILLE: NO. I JUST WANTED TO -- IT HAS BEEN AN AMAZING AMOUNT OF WORK THAT THE TEAM HAS UNDERGONE. AND FOR THAT I AM JUST VERY THANKFUL AND JUST VERY PROUD OF ALL THE WORK THEY'VE DONE. SO IT'S A HUGE CHALLENGE TO GET ALL THE DATA TOGETHER. KUDOS TO YOU, SHYAM. AND TO BE ABLE TO PRESENT THIS IN A MANNER THAT EVEN ME AS A NONSCIENTIST CAN UNDERSTAND AND RELATE TO. SO THANK YOU.

AND I WANTED TO ECHO MONICA'S COMMENT. I THINK ARRIVING AT HOW WE PRIORITIZE DISEASE RELEVANCE AND HOW WE COME ABOUT GETTING TO WHAT NUMBER, WHAT THE NUMBER X MEANS OR THE LETTER X MEANS, WHAT NUMBER THAT RELATES TO I THINK IS GOING TO BE A REALLY BIG CHALLENGE. AND SO THOSE ARE JUST SOME QUESTIONS THAT I WOULD HAVE MOVING FORWARD.

DR. CANET-AVILES: I APPRECIATE THIS. I THINK -- THANK YOU, MARIA. THE DEFINITION OF THE X IS STILL BEING REFINED IN COLLABORATION WITH FEEDBACK FROM BOARD MEMBERS. AND WE WOULD APPRECIATE, LIKE, IF YOU WANT TO SEND US EMAILS OR CONNECT WITH US TO DISCUSS THIS, THIS WILL EVOLVE AS THE STRATEGIC ALLOCATION FRAMEWORK PRIORITIZATION

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

PROCESS CONTINUES. AND WE EXPECT THAT WE WILL HAVE THE COMPLETE INFORMATION TO OUR SEPTEMBER MEETING, THE FIRST ONE, THE SCIENCE SUBCOMMITTEE/NEURO TASK FORCE, WE COULD HAVE SOME NUMBERS. I THINK IT'S EASIER TO ADD NUMBERS TO THIS INCOGNITO, THIS X FOR THE CLINICAL ACTUALLY. IT'S HARDER FOR THE EARLIER STAGES IN TERMS OF TECHNOLOGIES THAT WE WILL VALIDATE OR TECHNOLOGIES THAT ARE IDENTIFYING NEW TARGETS OR BIOMARKERS. AS WE ALL KNOW, THAT'S VERY HARD, ESPECIALLY VALIDATING THEM. SO WE WANT TO BE VERY MINDFUL THE WAY WE DO IT.

AND I DON'T KNOW IF I GOT THE QUESTION RIGHT. AND, SHYAM, FEEL FREE. SHYAM WAS THE HOLDER OF THE BATON FOR ALL THE EXTERNAL DATA. BUT IN TERMS OF THE DISEASES, WHILE DISEASES WITH LARGE PATIENT POPULATIONS AND SIGNIFICANT IMPACT ARE CERTAINLY IMPORTANT, CIRM WILL ALSO PRIORITIZE MEDICAL NEEDS AND INNOVATIVE APPROACHES THAT CAN HAVE A TRANSFORMATIVE IMPACT. AND WHAT WE ARE TALKING HERE WAS MORE AT THE LEVEL OF HOW WE WERE THINKING IN TERMS OF THE RECOMMENDATIONS. BUT EACH PROJECT, WHEN IT'S EVALUATED, IT'S EVALUATED IN ITS OWN MERITS, INCLUDING THE POTENTIAL FOR BROAD APPLICABILITY AND SIGNIFICANT PATIENT IMPACT.

WE JUST WANTED TO HAVE AN IDEA THROUGH ALL

THE DATABASES THAT YOU'VE SEEN, THAT WE ARE NOT SUGGESTING A LIST OF PRIORITY DISEASES. WE JUST WANTED TO SHOW CIRM IS DERIVED FROM PROP 71 AND PROP 14, WHICH IS FOR DISEASES THAT AFFECT CALIFORNIANS. WE WANTED TO HAVE AN IDEA WHAT ARE THE DISEASES? WHAT'S THE AMENABILITY? WHERE ARE THE GAPS? WHAT CAN WE DO TO MOVE THINGS FORWARD TO HAVE AN EFFECT ON CALIFORNIANS?

CHAIRMAN FISCHER-COLBRIE: OKAY. BEFORE WE GET BACK TO CAROLYN'S QUESTION, I SEE MONICA AND THEN FRED FISHER.

DR. CARSON: I JUST WANT TO DO ONE QUICK CLARIFICATION OF ONE THING. THAT WAS REALLY BEAUTIFUL. THANK YOU FOR CLARIFYING THAT.

I WOULD SUGGEST THAT CLINICAL DATA IS NOT AS EASY AS SAID. OUR DATABASES ARE STRUCTURALLY BIASED. AND THE ALGORITHMS FOR MEDICAL TREATMENT, THE WAY WE RECORD PEOPLE'S COMPLAINTS, AND WE BEND THEM. WHEN I STARTED IN THE FIELD, FOLKS FROM LATINX, LATINA, LATINO GROUPS DON'T GET MULTIPLE SCLEROSIS. IT'S BECAUSE OF HOW WE RECORDED THINGS AND THE PRESUMPTIONS THAT THEY'RE IN. SO THIS IS WHAT I'M SAYING.

IN MY FIELDS, AND I'M PART OF ANOTHER GROUP IN MY PROFESSIONAL LIFE, THESE DATABASES ARE

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

DIFFICULT. SO I DON'T THINK IT'S AS EASY, AND I THINK THAT'S JUST WHY I WANT IT ON THE RECORD. BUT WE'RE NOT GOING TO SOLVE IT HERE. IT'S JUST AN AWARENESS ISSUE.

CHAIRMAN FISCHER-COLBRIE: GREAT. FRED.

DR. FISHER: YES. I WANT TO ADD MY GRATITUDE TO THE TEAM FOR PUTTING THIS REPORT TOGETHER. IF I UNDERSTAND CORRECTLY, THE GOAL IS TO SHIFT, AT LEAST IN SOME WAY, TOWARD LATER STAGE RESEARCH FUNDING. AND IF THAT'S TRUE, THE LATER YOU GO, THE MORE EXPENSIVE IT GETS. AND SO THE PACE AT WHICH WE ARE CONSUMING FUNDS WOULD LIKELY INCREASE AS WE SHIFT OUR PRIORITIES TOWARD LATE-STAGE SUPPORT OF POTENTIAL DRUG CANDIDATES AND WORKING WITH DRUG COMPANIES. AND WE JUST MAY WANT TO CONSIDER THE FINANCIAL IMPACT OF MOVING TO SUPPORTING LATE-STAGE DEVELOPMENT, WHICH HAS BEEN PRIMARILY SUPPORTED BY THESE COMMERCIAL COMPANIES GOING OUT AND GETTING MONEY.

AND IF WE ARE GOING TO BECOME A PLAYER IN THAT SPACE, WE'RE GOING TO BE SPENDING A LOT OF MONEY, A LOT MORE THAN WE HAVE ON A PROJECT-BY-PROJECT BASIS. SO JUST -- I DON'T KNOW WHAT TO DO ABOUT THAT, BUT JUST WANTED TO PUT IT OUT THERE.

CHAIRMAN FISCHER-COLBRIE: I THINK IT'S A VERY RELEVANT POINT, FIRST OF ALL. SECOND, I THINK WITHIN THE DISCUSSION POINTS HERE, ONE OF THE KEY FRAMEWORK ELEMENTS HAS TO DO WITH THE FACT OF INVOLVING A LOT OF DIFFERENT GROUPS, FIRST OF ALL. AND SECOND, INCLUDING DRAGGING IN LARGE PHARMA AT AN EARLIER STAGE IN THE PROCESS WITH THE CONCEPT BEING THAT WE COULD THROW A TON OF MONEY AT STUFF, AND IT'S GOING TO BE A DROP IN THE BUCKET FOR ACTUALLY ULTIMATELY ACHIEVING COMMERCIALIZATION OF SOME THERAPEUTIC, LET'S SAY.

AND SO WITHIN THAT PURVIEW, THEN, CAN CIRM BE THE SPARK PLUG TO PULL THIS ALTOGETHER AND TO MAKE IT ACTUALLY HAPPEN THAT OTHERWISE WOULD NOT HAPPEN ON ITS OWN. BUT CLEARLY, FRED, YOU'RE SPOT ON. AND WHATEVER ALLOCATION MECHANISMS ARE DETERMINED HERE HAS TO BE DONE IN THE REVIEW OF WHAT ARE THE DOLLARS ALLOCATED TO THAT? AND IS THAT OUR REAL INTENT RELATED TO THAT? SO YOUR QUESTION IS FRONT AND CENTER AS PART OF THIS PROCESS OVERALL FROM MY PERSPECTIVE.

DR. FISHER: THANK YOU.

DR. CANET-AVILES: SO CAN I JUST CLARIFY, IF YOU DON'T MIND? I THINK THIS IS A VERY GOOD COMMENT, BUT I JUST WANT TO MAKE TWO POINTS CLEAR.

ONE IS OUR GOAL IS NOT TO MOVE TOWARDS THE LATER STAGES. WE'RE NOT DEEMPHASIZING BASIC RESEARCH. WE ARE STREAMLINING THINGS AND FOCUSING. SO STREAMLINING MEANS FOR DISCOVERY. AS WE SHOWED, WE COULD BE GOING THROUGH THE MULTIDISCIPLINARY. WE COULD FOCUS ON BOTTLENECKS THROUGH TECHNOLOGY PLATFORMS. BUT WE WOULD SELECT, IN COLLABORATION WITH INDUSTRY, THE MOST RELEVANT BOTTLENECKS AND THE THINGS THAT WE HAVE RESOURCES TO LEVERAGE IN CALIFORNIA. AND WE WOULD ALIGN THIS WITH OUR DEVELOPMENT PIPELINE.

FOR WHAT WE PRESENTED TODAY, THE GOAL IS NOT TO MOVE TOWARDS THE LATER STAGES AND INVEST MORE. WE HAVE RECEIVED, AND I WAS MISTAKEN, NOT CLIN4, BUT FROM THE CLIN2 APPLICANTS, WE'VE RECEIVED FEEDBACK THAT THERE IS A NEED FOR CLIN2 AWARDEES, IN ORDER TO SUPPORT BLA READINESS, THE COSTS ARE HIGHER, AND THE ACTIVITIES THAT WE WOULD NEED TO FIND COULD INVOLVE SOME ASPECTS LIKE LATER STAGE PRODUCT DEVELOPMENT, PRECOMMERCIAL MANUFACTURING, AS WELL AS CLINICAL AND NONCLINICAL RESEARCH POTENTIALLY.

SO WE ARE ENABLING, AS WE HAVE A PIPELINE OF POTENTIAL PROGRAMS THAT ARE GOING TO BE BLA READINESS, APPROVAL, WE ARE ALLOWING FOR THOSE

POTENTIAL APPLICANTS TO BE SUCCESSFUL. AND IT COULD BE AT A STAGED TYPE OF SCENARIO, BUT THAT WOULD BE FOR THINGS THAT WE COULD PRIORITIZE.

AND SHYAM HAS HIS HAND RAISED, AND HE'S BEEN DEVELOPING THIS. AND I ALSO WOULD WELCOME ABLA'S COMMENTS. PLEASE GO AHEAD, SHYAM.

DR. PATEL: THANKS, ROSA. I JUST WANTED TO REITERATE THAT POINT AS WELL AS THE OVERALL GOAL. SO WITH RESPECT TO THE LATER STAGE DEVELOPMENT, THIS IS FOR THE CLIN4 WHERE EXISTING CLIN2 AWARDS HAVE SOME GAPS THEY NEED TO OVERCOME IN ORDER TO GET TO BLA READINESS. AND AS WE KNOW FROM CELL AND GENE THERAPY DEVELOPMENT MORE BROADLY, THOSE CAN BE SUBSTANTIAL. AND SO THIS IS ADDRESSING A NEED IN OUR OWN PORTFOLIO WHERE THERE MIGHT NOT BE OTHER RESOURCES THAT SOME OF THESE PROGRAMS, PARTICULARLY THOSE IN THE RARE DISEASE SPACE, CAN TAP INTO OUTSIDE OF CIRM. SO THAT'S REALLY THE INTENT IS TO SUPPORT THOSE PROGRAMS MORE FULLY FOR THE CLIN4.

THE OTHER GOAL, I JUST WANT TO CLARIFY. SO WE'VE BEEN THINKING ABOUT THIS AS THE IMPACT OF CIRM WITH THE PROPOSITION MONEY UP UNTIL THE LAST AWARD IS EXECUTED. AND SO IN THAT SENSE, IF WE'RE GOING TO BE FOCUSING ON THAT, CAN WE DO THINGS ALONG THE SPECTRUM OF THERAPEUTIC DEVELOPMENT THAT COULD

RESULT IN HIGHER EFFICIENCY OF CANDIDATES GOING TO CLINICAL DEVELOPMENT AND THEN DEMONSTRATING SOME SORT OF CLINICAL PROOF OF CONCEPT THAT CAN THEN PROGRESS THEM INTO LATE-STAGE DEVELOPMENT. SO WE'RE ADDRESSING THINGS ALONG THE WAY TO GET BETTER CANDIDATES INTO LATER STAGE CLINICAL DEVELOPMENT, BUT NOT NECESSARILY SUGGESTING THAT WE PRIORITIZE ONLY LATE-STAGE CLINICAL DEVELOPMENT IN THAT SPACE.

DR. CANET-AVILES: THANK YOU, SHYAM. VERY WELL SAID. YEAH.

DR. FISHER: THANK YOU. SO I'M TRYING TO PUT THIS IN THE VERNACULAR THAT I'M MORE FAMILIAR WITH, WHICH IS LOOKING AT THE DRUG DEVELOPMENT PIPELINE AND FIGURING OUT WHERE WE'RE DEPLOYING OUR FUNDS. AND IT SEEMS LIKE WE'RE TALKING ABOUT A VALLEY OF DEATH FUNDING TO GET A PROJECT OVER TO THE POINT WHERE THEY MAY BE ABLE TO ATTRACT MORE COMMERCIAL MONEY. AND THAT'S AN EXPENSIVE PROPOSITION. IT'S WHY A LOT OF COMPANIES FAIL, BECAUSE THEY CANNOT ATTRACT THE MONEY. BUT IT'S A SIGNIFICANT AMOUNT OF MONEY.

AND I WOULD LOVE TO SEE A GRAPHIC THAT'S DIFFERENT THAN THE ONE THAT YOU PUT UP WHICH IS SORT OF CIRM RELATED. I WOULD LOVE TO SEE A GRAPHIC THAT SORT OF DEPLOYED THESE INITIATIVES AND WHERE THEY

ARE TARGETED IN THE DRUG DEVELOPMENT PIPELINE. BECAUSE THAT WOULD HELP ME CONTEXTUALIZE WHAT WE'RE REALLY TALKING ABOUT IN TERMS OF WHERE OUR MONEY IS GOING TO ACTUALLY GO. SO IF THAT'S POSSIBLE FOR SOME FUTURE MEETING OR EVEN BEFORE, I'D APPRECIATE THAT.

DR. CANET-AVILES: YEAH. I'M NOT SURE IF -- ABSOLUTELY. WHAT I WAS WONDERING IS IF THIS -- LET ME JUST GO BACK TO THE SLIDE THAT SHOWS THE -- ONE SECOND, FRED. IF IT'S SOMETHING -- I JUST WANT TO MAKE SURE THAT WE HAVE IT READY FOR THE NEXT MEETING. SO IN THIS SPECIFIC GRAPHIC, IT BASICALLY PORTRAYS THAT IN THE DISC2, TRAN1, 2, 3, 4, CLIN1, AS ONE OF THE CHANGES WE WOULD COMBINE THIS AND PROBABLY HAVE JUST TWO PROGRAMS. ALSO IT COULD HAVE A PRIORITIZATION FOR DISEASES AFFECTING CALIFORNIANS, AND THAT COULD BE -- WHEN THE RUBBER HITS THE ROAD, IT'S GOING TO BE IN THE SPECIFIC CRITERIA FOR REVIEW AND ELIGIBILITY. SO THAT'S GOING TO COME WHEN WE BRING THE CONCEPT.

AND I THINK WHAT WE ARE DOING -- YES. SO THAT'S NO. 1. SO THIS IS ONE OF THE RECOMMENDATIONS. THE OTHER RECOMMENDATION THAT WE BROUGHT IN WAS TO INCREASE CLIN2 FUNDING TO PROVIDE

NOVEL -- WHAT WAS IT? WHAT'S THE NAME?

DR. CREASEY: PLATFORM?

DR. CANET-AVILES: THE PLATFORM FORMAT TRIALS, TO BE ABLE TO -- THE MASTER PROTOCOLS FOR MULTIPLE THERAPIES. SO THAT'S NO. 1. RIGHT NOW WE DO SINGLE THERAPIES. AND THEN THERE IS THE FUNDING FOR THE RARE-DISEASE PILOT PLATFORM, WHICH ALSO COULD BE AROUND HERE AS WELL WITHIN CLIN2. AND THEN WE ASK THE CLIN4 FUNDING TO PROVIDE FOR MORE FUNDING. HOWEVER, THIS IS GOING TO BE ONLY ACCESSIBLE TO SUCCESSFUL CLIN2S THAT ARE READY FOR BLA-READY ACTIVITIES. AND OF THOSE, THE BOARD KNOWS FROM THE CLOSED SESSION HOW MANY WE HAVE FOR THAT.

WE HAVE TWO HANDS OPEN, AND I WOULD LIKE TO LEAD TO MY COLLEAGUES SHYAM AND ABLA.

DR. PATEL: YOU WANT ME TO GO FIRST, ABLA?

DR. CREASEY: IT'S OKAY. GO AHEAD. YOU WERE AHEAD OF ME.

DR. PATEL: THANK YOU. AND SO JUST WANT TO SUPPORT ROSA'S COMMENTS AND POINT OUT THAT THE TRADITIONAL DEVELOPMENT PATHWAY THAT, FRED, YOU RIGHTLY ASKED ABOUT IS SHOWN HERE AS WELL. IT'S A LITTLE BIT HIDDEN. SO IF YOU LOOK DOWN BELOW, THE SINGLE PRODUCT CANDIDATE PRE-IND MEETING, IND APPROVAL, SO ESSENTIALLY WHAT WE'RE SHOWING HERE IS

THAT THE DISCOVERY PHASE ACTIVITIES, THE PRECLINICAL VALLEY OF DEATH ACTIVITIES, IND FILING, AND THAT INITIAL CLINICAL TRIAL, THOSE ARE ALL THE ACTIVITIES UP TO THE END OF PHASE 2 MEETING OR EQUIVALENT. SO THOSE ARE ALL THE TRADITIONAL VALLEY OF DEATH ACTIVITIES WHERE YOU HAVE PRECLINICAL INVESTMENT. AND MOST OF OUR RECOMMENDATIONS ARE IN THAT RANGE OF ACTIVITIES BECAUSE THAT'S PREDOMINANTLY WHERE THE CIRM PORTFOLIO IS ALSO FOCUSED.

SO WE'RE HERE PROPOSING TO MAKE SOME CHANGES THAT WILL HELP CREATE MORE EFFICIENCIES AS WELL AS TAKE ADVANTAGE OF MULTIPLE APPROACHES AND MULTIDISCIPLINARY APPROACHES FOR THE DEVELOPMENT ALONG THAT PARADIGM.

SO BASICALLY JUST MAKING IT MORE EFFICIENT IN THE WAY THAT WE FUND THESE PROGRAMS AT THE STAGE WE'RE CURRENTLY FUNDING THEM AT, WHICH IS THAT PRECLINICAL AND EARLY CLINICAL DEVELOPMENT.

DR. CREASEY: JUST TO ECHO WHAT ROSA AND SHYAM SAID, IN FACT, WE ALREADY HAVE DATA WHERE SOME OF OUR GRANTEES ARE NOT NEEDING AS LONG AS THE AMOUNT OF TIME IN ORDER TO STAY IN A DISC2 OR A TRAN1 TO GET TO THE PRE-IND MEETING. THEY'RE JUMPING FAST TOWARDS FILING THEIR IND AND MOVING INTO A POTENTIAL CLINICAL TRIAL.

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

SO INSTEAD OF KIND OF BOXING THEM INTO YOU'VE GOT TO BE IN TRAN1 FOR X NUMBER OF MONTHS OR SO MANY YEARS FOR CLIN1, ET CETERA, IT WILL BE IMPORTANT TO RECOGNIZE THAT THE TREND IS THAT THEY'RE NOT NEEDING AS MUCH TIME AND MORE DATA IN ORDER TO GET TO A CLINICAL TRIAL. SO GIVEN THAT INFORMATION, THAT ALLOWS US TO BECOME MORE EFFICIENT, NOT NECESSARILY INCREASE THE AMOUNT OF FUNDING. WE'RE STILL -- THE ONES WHO ARE ALREADY IN THE PIPELINE IN A CLIN1 OR A TRAN1 CAN CONTINUE, BUT WE'RE PROVIDING THE OPTION OF HAVING THAT FLOW FROM DISC2 TO FILING AN IND AND GETTING A CLINICAL TRIAL GOING CAN BE ALLOWED IN ORDER, SINCE WE'RE SEEING IT HAPPENING IN FRONT OF US. AND THAT'S FROM A PRACTICAL VIEWPOINT.

WE RECOGNIZE THE IMPORTANCE ALSO OF NEEDING TO CHANGE OR AT LEAST STAY ABREAST OF WHAT THE REGULATORS ARE DOING RELATIVE TO CLINICAL DESIGN. AND IN SOME WAYS, IT WILL HELP OUR GRANTEES GET CLOSER TO IDENTIFYING THE RIGHT CANDIDATE TO MOVE FORWARD USING A CLIN2 THAT HAS THESE MASTER PROTOCOLS, WHETHER IT IS A UMBRELLA TRIAL, BASKET TRIAL, OR PLATFORM TRIAL.

SO THE KEY HERE IS NOT REALLY TO EXPEND OUR DOLLARS, BUT HOW TO STAY CURRENT WITH THE

REGULATORY INNOVATION AS WELL AS WITH THE NEEDS OF OUR GRANTEES. AND, AGAIN, I THINK WE NEED TO STAY CLOSE TO SORT OF LIKE ADAPTING TO WHAT IS HAPPENING IN OUR INDUSTRY. AND WE RECOGNIZE THE FACT THAT WE DON'T REALLY WANT TO SPEND OUR MONEY WITHOUT UNDERSTANDING THE TRENDS THAT WE'RE SEEING.

SO THANK YOU FOR YOUR COMMENT, FRED.

CHAIRMAN FISCHER-COLBRIE: WHAT I'D LIKE TO TURN THE Q AND A OVER TO ROSA AND LET YOU GET BACK TO MONICA'S QUESTION, WHICH HAD TO DO WITH SOME CONTEXTUAL FRAMING. MONICA, IF YOU WANT -- I'M SORRY. CAROLYN'S QUESTION. MY MISTAKE. CAROLYN'S INITIAL QUESTION RELATED TO SOME CONTEXT AROUND DEFINITIONAL ASPECTS. SO, ROSA, I THINK YOUR INITIAL SLIDE. BUT I'LL TURN THE Q AND A OVER TO YOU. SO I DON'T NEED TO MODERATE THAT.

DR. CANET-AVILES: YOU TURNING IT TO ME? I THOUGHT YOU WERE TURNING IT TO CAROLYN. YES.

SO FROM MY UNDERSTANDING, CAROLYN, YOUR INTENTION WAS TO GO OVER THESE QUESTIONS AND MAKE SURE THAT WE HAVE COVERED WHAT WE -- THAT THESE QUESTIONS ARE SUFFICIENT OR IF THERE IS ANYTHING ELSE THAT THE BOARD IS THINKING THAT WE SHOULD BE THINKING ABOUT ANSWERING. SORRY. IT'S MOVING.

DR. MELTZER: EITHER THE HIGH-LEVEL

QUESTIONS OR THE APPROACH. YOU'VE CONVEYED THE DATA IN GREAT DEPTH. JUST WANTED TO SEE IF THERE WAS FURTHER INPUT. IT SOUNDS LIKE WE'VE ALREADY HAD A RICH CONVERSATION, BUT IT WAS JUST A SUGGESTION.

DR. CANET-AVILES: AND I COULD GO THROUGH OUR RATIONALE. WE HAD MANY MORE QUESTIONS. I CAN ALSO GO THROUGH THE PROCESS HOW WE DID THIS. I DON'T KNOW IF IT WOULD BE HELPFUL. THE WHOLE LT GATHERED FOR SEVERAL DAYS THROUGH A PERIOD OF A MONTH TO GO OVER, FIRST, DEFINING THE CATEGORIES AND THEN DEFINING THE IMPACT GOALS. AND THOSE WERE INITIALLY IMPACT GOALS THAT WE DEFINED, BUT WE HAVE THE FOUR CATEGORIES VERY WELL ESTABLISHED THROUGH THE STRATEGIC PLAN THAT WE ALREADY HAVE. AND THEN WE WENT INTO THINKING AND BRAINSTORMING ABOUT WHAT QUESTIONS AND WHAT SECTIONS COULD WE HAVE TO COVER IN ORDER TO FIGURE OUT HOW THESE RECOMMENDATIONS COULD BE JUSTIFIED IF WE MAKE THAT.

SO ONE OF THEM, THE FIRST ONE IS THE CURRENT PORTFOLIO. AND MAYBE HERE WE DIDN'T SAY IT, BUT IT WAS IMPLICIT THAT NOT ONLY THE CURRENT PORTFOLIO, BUT WE ALSO DID LANDSCAPE ANALYSIS OF THE INDUSTRY, ON THE PORTFOLIO, THE GENERAL PORTFOLIO, ON RARE DISEASES AND THE REGULATORY LANDSCAPE AS WELL. HOW MANY CELL AND GENE THERAPIES HAVE BEEN

APPROVED? WHICH DISEASES? HOW HAD IT TO CHANGE? ALL THOSE THINGS WERE TAKEN INTO ACCOUNT. THESE ARE VERY HIGH LEVEL, REPRESENTING WHAT WE'VE SHOWN TODAY, BUT THERE WAS A LOT MORE GRANULARITY.

SO IN TERMS OF -- IF WE WANT TO ADVANCE THESE X RARE DISEASES PROJECTS TO BLA, WHAT DO WE HAVE IN OUR PORTFOLIO? RIGHT. AND ALSO WE WANT TO KNOW HOW EFFECTIVE IS OUR PIPELINE. HOW IS OUR PIPELINE GOING FROM DISCOVERY TO CLIN2? WHAT'S THE PROPORTION OF PROJECTS THAT GO FROM DISC2 TO TRAN, FROM TRAN TO CLIN1, CLIN1 TO CLIN2, AND HOW DOES THIS COMPARE TO THE INDUSTRY STANDARDS? RIGHT. AND ARE THERE ANY CHALLENGES THERE? SO THAT'S THE KIND OF THINGS THAT WE EVALUATED.

IN TERMS OF INFRASTRUCTURE UTILIZATION, WE LOOKED AT -- IF WE WANT TO DO THAT, IS THERE ANYTHING IN MANUFACTURING? MANUFACTURING, WE'VE ONLY HAD PHASE 1. SHYAM HAS BEEN LEADING THESE, AND HE'S NOW GOING TO PLAN FOR THE NEXT PHASE, RIGHT, SHYAM? BUT NOT ONLY THIS, BUT ALSO THE PATIENT SUPPORT INFRASTRUCTURE. AND THIS LINKS TO THE NEXT GOAL, GOAL 5, THAT WE WILL COME WITH IN SEPTEMBER. SO THINGS LIKE THAT JUST TO SHOW THAT IT'S ALL CONNECTED. RIGHT?

AND THEN WITH CLINICAL, THAT IS WHAT

DERIVED TO SOME OF THE OUTCOMES THAT ABLA WAS MENTIONING IN TERMS OF INCREASING THE FUNDING FOR SOME ACTIVITIES THAT ARE NOT CURRENTLY FUNDED THROUGH CLIN2 OR THROUGH CLIN4. RIGHT.

IN TERMS OF APPROACH, HOW WOULD WE HAVE TO DO THIS. ONE OF THE THINGS IS IN PART LIKE MORE OPERATIONAL OR HOW WE HAVE THINGS. BUT RIGHT NOW WITH THE DISCOVERY -- WITH THE PRECLINICAL RESEARCH, WE REALIZED THAT HISTORICALLY WE HAVE HAD THESE TWO, THE TRANS, THE CLIN1, BUT IS IT TIME FOR REEVALUATION? ALSO, WE WANT TO LOOK AT THE CURRENT PORTFOLIO AND MAYBE HAVE AN AUDIT OF THE CURRENT PORTFOLIO. I DON'T WANT TO SCARE ANYBODY, BUT WE DO NEED TO LOOK AT WHAT IS -- THERE ARE CLINICAL PROGRAMS THAT MAYBE WE NEED TO SAY, WELL, YOU'VE BEEN DOING THIS FOR A VERY LONG TIME. ARE YOU TACKLING THE RIGHT BOTTLENECKS HERE? ARE YOU REALLY LIKE GOING TO GET THERE? AND IF NOT, WE MIGHT HAVE MONEY TO INVEST IN THE KIND OF THINGS THAT WE ARE TRYING TO INVEST TO MOVE THE PIPELINE FORWARD.

SO THOSE ARE THE KIND OF THINGS THAT WE ARE GOING TO BE -- YES.

DR. MELTZER: I WASN'T QUESTIONING HOW ALL OF THE DATA WAS PUT TOGETHER TO ANSWER THESE QUESTIONS. JUST TO SEE IF THERE WAS FURTHER

FEEDBACK ON THE PRESENTATION AND ON MAYBE SOME OF THESE QUESTIONS AROUND PARTNERSHIPS, AROUND THE DATA CENTER, ALL OF THAT. BUT MAYBE IT'S NOT BEEN HELPFUL.

DR. CANET-AVILES: YOU WERE OPENING FOR OTHER MEMBERS OF THE BOARD, NOT TO PROVIDE THEIR INPUT, CAROLYN?

DR. MELTZER: YEAH. JUST TO SEE IF THERE WAS MORE INPUT.

DR. CANET-AVILES: AND I WAS ACTUALLY -- I'M SORRY. I WAS ACTUALLY JUST MENTIONING SO THAT PEOPLE COULD HAVE TIME TO THINK ABOUT WHAT THEY MIGHT WANT TO SAY AS WELL. SO I WAS GOING THROUGH THESE SO THAT THEY HAD A BIT MORE TIME. AND MAYBE BY ME EXPLAINING OUR PROCESS, IT COULD LEAD TO SOMEBODY THINKING, OH, THIS IS HOW WE CONNECT.

AND ONE OF MY COLLEAGUE -- ABLA WAS MENTIONING THAT WE WANT TO ACCENTUATE, AND J.T. ALSO MENTIONED, THAT THE DISCOVERY PART OF OUR PIPELINE IS, AS WE MENTIONED IN GOALS 1 AND 2, IS EXTREMELY IMPORTANT, RIGHT, AS WELL BECAUSE WE ARE NOT A VENTURE CAPITAL FIRM HERE. WHAT WE ARE IS A FUNDING AGENCY, AND WE NEED TO FIGURE OUT HOW TO STRENGTHEN OUR RESEARCH TO LEAD TO OVERCOMING BOTTLENECKS.

SOME OF THE THINGS THAT WE WILL LEAVE AS A LEGACY WILL NOT BE AN APPROVAL, BUT WILL BE A BIOMARKER THAT WILL HELP US ACCELERATE A CLINICAL TRIAL IN THE FUTURE. SOME OF THE BOTTLENECKS FOR SOME OF THESE NEURODEGENERATIVE DISEASES, WHICH MIGHT NOT BE AMENABLE TO CELL AND GENE THERAPIES, ARE THAT THEY ARE VERY LONG CLINICAL TRIALS. AND NOBODY CAN INVEST. THEY'RE VERY EXPENSIVE CLINICAL TRIALS BECAUSE WE DON'T HAVE THE RIGHT BIOMARKERS OR THE RIGHT BIOMARKERS TO STRATIFY OR WE ARE NOT GOING THROUGH THE RIGHT SYSTEM OR TARGET, RIGHT, OR DISEASE MECHANISM.

SO THOSE ARE THE KIND OF THINGS THAT CIRM ALSO SHOULD BE FOCUSING. AND ONE OF THE THINGS THAT, WE'VE HEARD IT LATELY, WE NEED TO MESSAGE THIS PROPERLY TO CALIFORNIA, RIGHT, BECAUSE THIS IS THE VALUE THAT CIRM WILL HAVE IN THE FUTURE AS WELL. AND WE HAVE TO BE ABLE TO SHOW THAT EARLIER RESEARCH, TRANSLATIONAL RESEARCH MIGHT NOT BE AT THE END OF CIRM PROPOSITION 14 LEADING TO AN APPROVAL SPECIFICALLY, BUT WE NEED TO INVEST BECAUSE THAT WILL HELP IN THE FUTURE.

SO I DON'T KNOW IF THERE IS INPUT IN THESE QUESTIONS AS CAROLYN WAS SUGGESTING. I GUESS WE DID A FANTASTIC JOB, NO, WITH THE QUESTIONS? FRED IS

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

GOING TO GIVE US SOME INPUT.

DR. FISHER: SOME MORE TO THINK ABOUT. SO WHEN I LOOK AT THIS, I'M WONDERING LIKE THE VERY FIRST QUESTION, WHAT PROPORTION OF THE CURRENT PORTFOLIO SUPPORTS RARE DISEASES? YOU SHOWED US A VERY COMPREHENSIVE SLIDE THAT BREAKS ALL THAT DOWN, BUT IT FORCES US TO ANSWER THE QUESTION FOR OURSELVES. AND AS BOARD MEMBERS, WE'RE NOT AS FAMILIAR WITH THIS DATA AND DON'T HAVE THE TIME TO ADD UP ALL THE BAR CHARTS. IT WOULD BE GOOD IF WE JUST HAD AN ANSWER.

AND THERE'S OTHER QUESTIONS THAT JUST SORT OF LEND THEMSELVES TO JUST IF WE HAVE THE ANSWER, LET'S PROVIDE IT BECAUSE WE DON'T WANT TO -- PEOPLE ARE GOING TO SEE THIS FOR THE FIRST TIME OR SECOND TIME OR THIRD TIME, BUT THEY'RE STILL NOT GOING TO BE ABLE TO MANAGE THE DATA IN THEIR HEAD.

DR. CANET-AVILES: YEAH. THAT'S A GREAT POINT, FRED. AND I APPRECIATE IT BECAUSE WE HAVE BEEN LOOKING AT THIS SO MUCH, THAT WE DON'T REALIZE THAT IT'S NOT -- IN MY NARRATIVE I MENTIONED WHAT IT WAS, BUT I THINK THIS IS A GREAT IDEA. WE SHOULD HAVE A LITTLE POP-UP HERE THAT SAYS IN THE EARLIER STAGES, DISC AND TRAN, PREVALENT DISEASES ARE MORE PREVALENT IN OUR PORTFOLIO. SO WE HAVE A 55 TO 45

PERCENT RATIO. SO 45 PERCENT IN RARE AND ULTRA-RARE DISEASE RESEARCH AND 55 PERCENT IN PREVALENT. AND THAT'S MOSTLY BECAUSE WHAT WE SHOWED IN DATA AND GOALS 1 AND 2, THERE ARE MODELS, STEM CELL MODELS FOR MANY DISEASES THAT ARE PREVALENT THAT WE CAN UTILIZE TO MODEL THE DISEASE AND DO MORE DISCOVERY AND VALIDATION OF FINDINGS IN THE EARLIER STAGES. NOW, THOSE DISEASES ARE NOT RIGHT NOW AMENABLE FOR CELL AND GENE THERAPIES. CELL AND GENE THERAPIES ARE OFTEN DESIGNED TO ADDRESS UNDERLYING GENETIC OR CELLULAR CAUSES OF DISEASES, WHICH ARE PARTICULARLY WELL-SUITED FOR RARE AND ULTRA-RARE CONDITIONS WHERE SPECIFIC MUTATION OR CELLULAR DYSFUNCTIONS ARE IDENTIFIED.

SO AS WE ADVANCE, WE WILL BE ABLE TO TACKLE MORE PREVALENT DISEASES. SO THIS IS WHAT THIS IS SHOWING. RIGHT? SO WE WILL ADD A LITTLE POP-UP THAT SAYS THE PROPORTIONS SO IT'S EASIER. AND WE WILL DO IT IN THE NEXT ONE AS WELL.

MARIA, YOUR HAND IS UP.

VICE CHAIR BONNEVILLE: I WANTED TO ASK QUESTIONS AROUND PARTNERSHIPS. CAN YOU GO BACK TO THE SLIDE?

DR. CANET-AVILES: YES.

VICE CHAIR BONNEVILLE: PARTNERSHIPS IS

ONE OF THE -- ARE STRATEGIC PARTNERSHIPS NECESSARY TO ACHIEVE THIS GOAL? I THINK THAT'S RHETORICAL, BUT I WOULD SAY, YES, ABSOLUTELY. AND IT'S -- WE'VE DONE A GOOD JOB IN THE PAST OF SORT OF IDENTIFYING AREAS WHERE WE COULD PARTNER. I THINK WE DO NEED A BETTER JOB MOVING FORWARD, AND I THINK THAT A SKILL SET OF SOMEONE BEING ABLE TO CONNECT THE DOTS OF CONSTANTLY COMBING THROUGH INFORMATION OF WHO'S DOING WHAT AND THEN RELATING IT BACK TO EITHER INITIATIVES OR POTENTIAL INITIATIVES THAT WE OURSELVES ARE UNDERGOING. SO I THINK THAT'S KEY MOVING FORWARD. I THINK PARTNERSHIPS ARE ABSOLUTELY KEY. ONE ALLOWS OTHER PEOPLE TO KNOW WHO WE ARE AND WHAT WE'RE DOING. SO FROM A PR PERSPECTIVE, SUPER VALUABLE. BUT THEN ALSO FROM A MONEY PERSPECTIVE, ALSO SUPER VALUABLE BECAUSE SOMEBODY ELSE HAS SKIN IN THE GAME AND ALSO EXTENDS OUR DOLLARS LONGER SO THAT WE CAN ENGAGE IN MORE RESEARCH AND ACTIVITIES THAT HELP MOVE THIS ALONG THE CONTINUUM. SO I'M A HUGE PROPONENT OF LOOKING FOR MORE OF THOSE PARTNERSHIPS.

DR. CANET-AVILES: YEP. THANK YOU, MARIA. THAT'S A GREAT POINT. J.T.

DR. THOMAS: YES. I WANT TO -- I'M FOCUSING ON GOAL 3 THERE. WE, AS EVERYBODY KNOWS,

RECEIVED A LETTER, VERY-WELL CONSIDERED LETTER FROM A GREAT MANY FROM THE DISEASE ADVOCATE AND PATIENT AREA THAT WAS CONCERNED ABOUT RARE DISEASE AND HOW WE WOULD BE FOCUSING ON THAT GOING FORWARD. AND I THINK, ABLA, IF YOU COULD GIVE A LITTLE EXTRA COLOR ON THAT FOR MEMBERS OF THOSE VERY IMPORTANT GROUPS TO LET THEM KNOW THE DIFFERENT WAYS THAT WE WILL BE CONSIDERING RARE DISEASE. I THINK THAT WOULD BE VERY HELPFUL. THANK YOU.

DR. CREASEY: OKAY. THANK YOU, J.T. YES. AGAIN, AS A RARE DISEASE PATIENT ADVOCATE MYSELF, I JUST WANT TO EMPHASIZE THAT WE WILL HAVE THREE DIFFERENT PATHWAYS TO ADVANCE RARE DISEASES. ONE IS THE CURRENT PORTFOLIO HAS A NUMBER OF RARE-DISEASE GRANTS THAT ARE ADVANCING TOWARDS LATE DEVELOPMENT AND POTENTIAL BLA'S. AND WE'RE GOING TO SUPPORT THEM WHOLEHEARTEDLY WITH THAT KIND OF CLIN4 TYPE OF GRANT WHERE WE'RE ADVOCATING FOR ENHANCING THE FUNDING FOR THAT PURPOSE.

WE FOUND OUT THAT IT'S PROBABLY -- THE BURDEN OF FILING THE BLA WITH THE CURRENT GRANTEES IS AROUND 25 MILLION. WE'RE SUPPORTING A CLIN4 WITH 12. AND SO FOR THAT REASON, WE'RE SAYING, OKAY. WE HEARD YOU, RARE DISEASE. WE'D LIKE YOU TO GET APPROVED. AND FOR THAT PURPOSE, WE'RE GOING TO SEE

IF WE CAN ENHANCE THE CHANCE FOR YOU TO DO THAT WITHOUT HAVING TO SPEND -- TO COME TO CIRM TWICE TO DO A CLIN2. AND THAT'S REALLY THE RATIONALE FOR ADVOCATING FOR GETTING CLIN4 FUNDING INCREASED.

THE OTHER IS THAT, AS YOU KNOW, WHEN IT COMES TO CLINICAL GRANTS, WE STARTED THE GRANTING PROCESS AGAIN FOR CLIN1S AND CLIN2S AT THE END OF JULY. AND THE ENTRY TO AN APPLICATION TO CIRM THROUGH THAT ROUTE IS WHOLEHEARTEDLY OPEN FOR RARE DISEASES AS WELL. AND SO PLEASE BE MINDFUL OF THAT. AND WHEN YOU'RE READY, GO AHEAD AND APPLY DESPITE THE FACT AT THIS TIME THE NUMBER OF MONTHS BEFORE ANYONE KNOWS WHETHER THEY GOT AWARDED THE GRANT OR NOT IS NOW PROLONGED BY ONE MONTH, BUT IT'S STILL WORTH IT. AND WE'RE READY TO EVALUATE WHATEVER DISEASE YOU'RE ADVOCATING FOR AND WHAT KIND OF GRANT ARE YOU PROPOSING.

THE THIRD PATH, WHICH IS THE PATH THAT WAS DISCUSSED A LITTLE BIT, IS ABOUT POTENTIALLY DEVELOPING A -- WELL, IT'S NOT POTENTIALLY. WE ACTUALLY HAVE PROGRESSED OUR THINKING THERE. WE'RE GOING TO DEVELOP A RARE-DISEASE PILOT AS A CONSORTIUM WHERE WE'RE GOING TO ENABLE THE DEVELOPMENT OF RARE DISEASES IN AN ACCESSIBLE, SCALABLE, AND SUSTAINABLE MANNER IN COLLABORATION

WITH MULTIPLE GROUPS OUTSIDE CIRM AS WELL AS WITH THE REGULATORS. AND THAT EXERCISE IS GOING TO ALLOW US TO BE ABLE TO INTEGRATE A NUMBER OF REALLY GOOD THINGS THAT THE REGULATORS HAVE ALREADY IDENTIFIED WHEN IT COMES TO REGULATORY INNOVATION PER A VARIETY OF GUIDANCE DOCUMENTS. FOR EXAMPLE, IF IT IS A RARE DISEASE THAT IS SERIOUS AND LIFE-THREATENING, THE PRECLINICAL PACKAGE DOESN'T HAVE TO BE LENGTHY. SO HOW CAN WE USE THAT IN THE DESIGN OF THE PLATFORM? I'M JUST GIVING YOU EXAMPLES.

THE OTHER WOULD BE, ONCE WE HAVE -- AS MANY OF YOU KNOW WHO ARE WORKING IN RARE DISEASES, WE RECOGNIZE THAT WHETHER IT'S THE BIOLOGICS BRANCH OF THE FDA OR THE DRUG SET BRANCH, THEY'RE BOTH ADVOCATING FOR DOING A RARE DISEASE NATURAL HISTORY STUDY OR A REGISTRY. AND YOU NO LONGER HAVE TO DO SHAM OR PLACEBO CONTROLLED TRIALS. SO WE'RE MINDFUL OF THAT AS WELL.

I JUST WANT TO GIVE YOU EXAMPLES OF WHY WE THINK THIS RARE DISEASE PILOT PLATFORM TYPE TECHNOLOGY AND APPROACH IS REALLY GOING TO BUILD ON A LOT OF ADVANTAGES THAT THE REGULATORS HAVE GIVEN US TO ALLOW US TO MOVE FORWARD IN A MORE EXPEDITIOUS MANNER AND SOLVE THE ISSUE WITH MANY OF THE RARE DISEASES, ESPECIALLY IF WE WERE TO START WITH THE

NEUROLOGICAL DISEASES WHICH MANY OF YOU HAVE ALREADY SHARED WITH US, THAT WHEN IT COMES TO RARE DISEASE, PROBABLY 80 PERCENT OF THEM ARE GENETIC AND MANY OF THEM ARE IN THE NEUROLOGICAL AREA.

AND SO IF WE WERE TO CAPTURE ALL WHAT WE HAVE LEARNED THUS FAR IN THAT KIND OF A PLATFORM TECHNOLOGY, THEN IT'S GOING TO ALLOW US TO ADDRESS THE NEEDS OF THE PATIENTS MUCH MORE QUICKLY, MOST LIKELY WITH EQUAL DOLLARS OR LESS DOLLARS PER GRANT IN ORDER TO ALLOW US, THEN, TO CREATE LIKE AN AVENUE FOR THEM DOING MORE THAN ONE PATIENT OR TWO PATIENT AT A TIME. WE CAN DO TEN AT A TIME, 20 AT A TIME OR HUNDRED AT A TIME.

SO THAT'S WHERE WE'RE HEADING. WE'RE NOT READY YET TO PUT TOGETHER A CONCEPT PLAN, BUT PUTTING ALL THESE AGGREGATE, WHETHER IT'S TECHNOLOGY INNOVATION, REGULATORY INNOVATION, AS WELL AS READINESS IN PULLING ALL THAT DATA TOGETHER WHERE EVERYONE SHARES THEIR DATA REGULARLY WITH EACH OTHER IS GOING TO ALLOW US, THEN, TO BE VERY MUCH THE REAL ADVOCATES FOR RARE DISEASE AND ALLOW US TO UTILIZE WHATEVER DOLLARS WE HAVE FOR RARE DISEASE AND COMMON DISEASES UTILIZING THE MANNER WHERE WHATEVER LESSONS WE LEARN FROM SUCH A PILOT CAN BE APPLIED FOR THE COMMON DISEASES AS WELL. SO IF WE WERE TO DEVELOP A

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

ROADMAP THAT SHOWS WE WERE ABLE TO PROBLEM SOLVE FOR LIKE A NUMBER OF THOSE RARE DISEASES AND WE IDENTIFY IN THE MEANTIME A TARGET FOR A COMMON DISEASE, CAN WE DO THE SAME FOR THE COMMON DISEASE?

SO JUST WOULD LIKE YOU TO THINK -- ALSO WHAT WE'RE ADVOCATING FOR IS TO UTILIZE WHAT WE BUILT IN TERMS OF OUR INFRASTRUCTURE, USE THE ALPHA CLINICS, OUR MANUFACTURING UNITS, ET CETERA, TO HELP US MOVE THE PROGRAMS IN A CONSISTENT MANNER HAND IN HAND WITH THE REGULATORS TO ALLOW THEM TO SUCCEED AND REACH THE PATIENTS.

SO I'M HAPPY TO ANSWER ANY QUESTIONS YOU HAVE RELATIVE TO, AGAIN, THE THREE DIFFERENT PATHS. AND ONCE WE ARE READY FOR THE PLATFORM TECHNOLOGY TYPE CONSORTIUM, HAPPY TO ENGAGE ALL OF YOU IN THE DISCUSSION WITH US.

DR. THOMAS: ROSA, I WOULD JUST ADD TO WHAT ABLA SAID, THAT, OF COURSE, RARE DISEASE APPLICATION, GRANT APPLICATIONS IN THE DISCOVERY AND TRANSLATIONAL PHASE OR THE CONDENSED NEW PRECLINICAL PHASE WILL CONTINUE APACE AS WELL.

DR. CREASEY: CORRECT. CORRECT. YEAH. I JUST WOULD LIKE -- I ALWAYS SAY SOMETHING ALONG THE LINES, THINK OF A CONVEYOR BELT. LOOK HOW THE AUTOMOBILE COMPANIES HAVE STARTED DOING -- PUTTING

TOGETHER THE CAR ENGINE, THEN LET'S SAY THAT ACTUALLY THAT ANALOGY WAS USED WITH US. THE FDA PUT TOGETHER THE CAR ENGINE, BUT WE NEED TO PUT TOGETHER THE -- WE KNOW HOW TO PUT TOGETHER THE DOORS AND THE TIRES ON SOME OF THOSE PLATFORMS. AND SO THAT'S WHAT WE'RE TRYING TO DO RIGHT NOW, BUT IN A VERY AMENABLE WAY THAT WILL BE PRACTICAL. AND, AGAIN, THAT WOULD ALLOW FOR US TO DO ACCESSIBLE, SCALABLE, SUSTAINABLE, AND AFFORDABLE RARE DISEASE THERAPY MODALITIES.

DR. CANET-AVILES: THANK YOU, ABLA.

DR. CREASEY: YOU'RE WELCOME.

DR. CANET-AVILES: SO I THINK, J.T. AND CAROLYN AND MARK, WE WERE IN THE FRAMEWORK OF THE QUESTIONS. IF THERE WAS ANY OTHER -- I CAN GO INTO GOAL 4 IF THERE ARE ANY OTHER COMMENTS, QUESTIONS, ADDITIONS TO THESE FRAMEWORK QUESTIONS TO MAKE SURE. AND I APPRECIATE VERY MUCH FRED'S SUGGESTIONS TO MAKE IT MORE LIKE PROCESSABLE AS WE ARE PRESENTING. THIS IS A LOT ON OF INFORMATION. AND AS WE MOVE FORWARD, WE ARE GOING TO HAVE SIX GOALS AT THE SEPTEMBER MEETING. AND THAT'S GOING TO BE QUITE DENSE. SO WE WANT TO MAKE SURE THAT WE HAVE THE INFORMATION IN A WAY THAT'S EASIER TO PROCESS.

MARK. NO? SO IF THERE ARE NO OTHER

QUESTIONS OR COMMENTS, WHAT WE CAN DO IS SHOW, IF IT'S OKAY WITH YOU, MARK, THE TIMELINE/NEXT STEPS AND WHERE WE ARE AND WHERE WE WILL BE SOON. SOUNDS GOOD?

CHAIRMAN FISCHER-COLBRIE: SURE.

DR. CANET-AVILES: GREAT.

CHAIRMAN IMBASCIANI: AND IF ANYBODY THINKS ABOUT QUESTIONS IN THE MEANTIME JUMP IN. THIS IS THE TIME TO ASK.

DR. CANET-AVILES: AND ALSO WE ARE AVAILABLE ANY TIME TO RECEIVE FEEDBACK ON THE NUMBERS OR HAVE A DISCUSSION BETWEEN NOW AND THE SEPTEMBER JOINT SCIENCE SUBCOMMITTEE AND THE NEURO TASK FORCE.

SO TODAY WE WENT THROUGH THE FEEDBACK ON GOAL 1, 2, INTRODUCED 3 AND 4, AND DISCUSSED THE RECOMMENDATIONS. AND AT THE SEPTEMBER NEURO TASK FORCE AND SCIENCE SUBCOMMITTEE, I BELIEVE -- CLAUDETTE, IT'S SEPTEMBER 13TH, CORRECT?

MR. TOCHER: THAT'S RIGHT.

DR. CANET-AVILES: THANK YOU, SCOTT. WE WILL HAVE THE FULL PRESENTATION, BUT WE WILL MAKE IT A LITTLE SHORTER THAN THE ICOC. WE ARE GOING TO PRESENT 1, 2, 3, 4 WITH THE FEEDBACK RECEIVED. AND THEN FOCUSED ON GOALS 5 AND 6. FIVE IS ACCESS AND

AFFORDABILITY, 6 IS PROVIDE AN OPPORTUNITY FOR ALL THAT STRONGLY FOCUSES ON THE EDUCATION RECOMMENDATIONS AND TRAINING PROGRAMS. AND THEN WE WILL DISCUSS THE OVERALL RECOMMENDATIONS AND ANY COMMENTS IN PREPARATION FOR THE SEPTEMBER ICOC. I ALSO BELIEVE, SCOTT, DO LET ME KNOW IF IT'S MY TASK TO SAY THIS OR IT'S MARK'S OR YOURS WITH REGARDS TO SEEKING AN ENDORSEMENT. IS THAT YOUR ROLE OR MARK'S?

MR. TOCHER: WELL, I SUSPECT THAT IT WOULD BE HELPFUL TO THE FULL BOARD TO HAVE A RECOMMENDATION, AN ENDORSEMENT, FROM THE JOINT SUBCOMMITTEES WITH REGARD TO THE GOALS. SO I THINK THAT WOULD BE HELPFUL AT THE CONCLUSION OF THE PROCESS TO SEEK THAT ENDORSEMENT.

DR. CANET-AVILES: THANK YOU. AND THEN IN TERMS OF TIMING, THIS IS THE MEETING WE ARE TALKING ABOUT THAT WE WILL BE SEEKING AN ENDORSEMENT IN PREPARATION FOR SEPTEMBER 26TH, ICOC, WHICH IS IN SAN DIEGO, CORRECT?

MR. TOCHER: CORRECT.

DR. CANET-AVILES: AND WE WILL ALL BE THERE IN PERSON TO PRESENT THIS AND OTHER THINGS, BUT THIS IS A VERY IMPORTANT PART OF OUR HISTORY, I THINK. AND WITH THAT, ANY OTHER QUESTIONS? I LEAVE

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

IT TO MARK TO CLOSE THE MEETING.

CHAIRMAN FISCHER-COLBRIE: WITH THAT, THERE'S OBVIOUSLY A LOT ON OF MATERIAL HERE. I WOULD REALLY ENCOURAGE YOU TO LOOK THROUGH IT AND TO GIVE IT CAREFUL CONSIDERATION. THIS IS A VERY IMPORTANT TIME TO BE ABLE TO ENSURE THAT THE PROPER QUESTIONS HAVE BEEN ASKED, THAT THE CONSIDERATION OF ADDITIONAL FEEDBACK IS TAKEN INTO CONSIDERATION. AND OBVIOUSLY WE HAVE ANOTHER BITE AT THE APPLE HERE IN SEPTEMBER. BUT I APPRECIATE BOTH YOUR COLLECTIVE WISDOM AND YOUR COLLECTIVE EFFORT ON BEHALF OF ENSURING THAT AS AN ORGANIZATION WE CAN MOVE FORWARD IN THE BEST WAY WE POSSIBLY CAN. SO I WILL BE VERY MUCH -- I'M VERY, VERY THANKFUL AND APPRECIATIVE OF YOUR EFFORTS IN THIS OVERALL PROCESS. SO THANK YOU VERY MUCH.

MR. TOCHER: AND, MARK, BEFORE WE ADJOURN, WE'LL JUST WANT TO SOLICIT ANY PUBLIC COMMENT ONCE THE BOARD IS FINISHED.

CHAIRMAN FISCHER-COLBRIE: ANY OTHER QUESTIONS OF THE BOARD BEFORE WE OPEN IT UP FOR PUBLIC REVIEW AND COMMENT?

DR. FISHER: I JUST WANT TO SAY THANK YOU, MARK, FOR YOUR LEADERSHIP IN MOVING ALL OF THIS FORWARD. IT'S TERRIFIC.

CHAIRMAN FISCHER-COLBRIE: WELL, THANKS, FRED. I'M DOING NOTHING. THE TEAM IS UNBELIEVABLE. SO IT'S FUN TO SURF THE WAVE HERE. SO THANK YOU.

AND WITH THAT -- BRENDA.

DR. PORTER: I'M NOT ON THE BOARD. SO ARE YOU READY FOR PUBLIC COMMENTS?

CHAIRMAN FISCHER-COLBRIE: PUBLIC COMMENT. YEAH. HOLD ON JUST A SECOND. ANY LAST MINUTE COMMENTS OR QUESTIONS FROM THE BOARD? AND THEN, CLAUDETTE, IF YOU WOULD LET US KNOW WHO'S IN THE SEQUENCE FOR PUBLIC COMMENT.

MS. MANDAC: WE'RE STARTING WITH THE TWO WE HAVE IN THE ROOM, WHICH ARE NASHA AND LEAH. AND THEN WE'LL MOVE ON TO BRENDA WHO'S ON ZOOM.

EVERYONE HAS THREE MINUTES. I WILL KEEP TIME. YOU WILL BE ABLE TO SEE IT IN THE ROOM ON THE SCREEN AND ALSO ON ZOOM.

CHAIRMAN FISCHER-COLBRIE: CLAUDETTE, I'LL LET YOU CONTROL THE FLOW ON THAT. SO THANK YOU.

MS. MANDAC: THANKS, MARK.

MS. FITTER: I HOPE YOU GUYS CAN HEAR ME. CAN YOU HEAR ME? OKAY. ALL RIGHT. SO THANK YOU SO MUCH. AND THANK YOU, JON, ABLA, AND ROSA, FOR THE WORDS YOU SAID ABOUT RARE DISEASES AND YOUR WORK IN THIS AREA AND FOR ENGAGING WITH US. WE REALLY

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

APPRECIATED THAT.

MY NAME IS NASHA FITTER. I'M A CALIFORNIA RESIDENT, TAXPAYER, AND MOTHER OF A DAUGHTER LIVING WITH AN ULTRA-RARE DISEASE CALLED FOXG1 SYNDROME. AND THIS CONDITION DOES HAVE THE POTENTIAL TO BE TREATED WITH A GENE THERAPY. I AM HERE REPRESENTING ALL CALIFORNIA FAMILIES WITHIN THE ULTRA-RARE DISEASE COMMUNITY WHO ARE TIRELESSLY WORKING TOWARDS CREATING TREATMENTS. FOR US SUPPORT FROM CIRM IS VITAL AS FEDERAL, PHARMA, AND VC FUNDING IS ALMOST NONEXISTENT FOR OUR CONDITIONS. THAT LEAVES THE JOB OF FUND-RAISING UNFORTUNATELY TO PATIENT ADVOCACY GROUPS LIKE THE ONE I LEAD.

AND I WILL TELL YOU, DESPITE MY EXTENSIVE PROFESSIONAL EXPERIENCE IN FUND-RAISING AND NAVIGATING CAPITAL MARKETS, I HAVE FACED A REALLY HARSH REALITY, THAT IT IS BRUTALLY HARD TO RAISE MONEY FOR ULTRA-RARE CONDITIONS. JUST THIS WEEK A SENIOR BIOTECH EXECUTIVE TOLD ME, AND I QUOTE, "WE'RE NOT INVESTING IN ULTRA-RARE ANYMORE. OUR LAST PROGRAM DIDN'T MAKE ENOUGH MONEY. WE'RE GOING TO FOCUS ON MUCH LARGER RARE DISEASES." YET AS PARENTS WE HAVE NO CHOICE. WE ARE NOT GOING TO LET OUR CHILDREN DIE OR HAVE A LIFETIME OF SUFFERING.

OUR FOUNDATION UNITED OUR COMMUNITY. WE

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

INVESTED IN BASIC SCIENCE. WE BUILT ESSENTIAL RESOURCES LIKE A PATIENT REGISTRY, LIKE A NATURAL HISTORY STUDY. WE'VE RAISED FUNDS THROUGH GRASS ROOTS EFFORTS, AND WE HAVE PUBLISHED DATA ON OUR GENE THERAPY PRECLINICAL TRIALS.

BUT NOW WE'RE AT A PIVOTAL POINT. WE HAVE AN EXTREMELY PROMISING NEW PROGRAM THAT'S READY TO ENTER GLP TOXICOLOGY. THE NEXT STAGE IS CLINICAL TRIALS. AND AS YOU ALL KNOW, THEY COME WITH A PRICE TAG OF $10 MILLION, AN AMOUNT THAT IS SIMPLY BEYOND OUR NETWORK'S FAMILY AND FRIENDS REACH.

LIKE SO MANY OTHERS, WE FACE THE THREAT OF SINKING INTO THE VALLEY OF DEATH AND NOT BECAUSE OUR SCIENCE HAS FAILED, BUT BECAUSE OF A LACK OF FUNDING.

CIRM IS THE BEST AND PERHAPS THE ONLY AVENUE FOR FUNDING THAT SMALL BIOTECH COMPANIES AND PATIENT ADVOCACY GROUPS LIKE OURS CAN TURN TO. WHILE LARGER CONDITIONS CONTINUE TO RECEIVE BILLIONS OF DOLLARS IN PHARMA AND VC SUPPORT, ULTRA-RARE CONDITIONS LIKE OURS ARE LEFT BEHIND. WE UNDERSTAND THAT CIRM NEEDS TO MAXIMIZE TAXPAYER DOLLARS. AND, THUS, I JUST URGE YOU TO THINK ABOUT THIS IN THE FOLLOWING WAYS.

FIRST, SHOULD OUR TAXPAYER DOLLARS BE

INVESTED IN AREAS IGNORED BY CAPITAL MARKETS? SHOULD TAXPAYER DOLLARS BE USED FOR CONDITIONS THAT COULD FIND FUNDING ELSEWHERE?

SECOND, THE MAJORITY OF ULTRA-RARE DISEASES ARE MONOGENIC. THEY ARE EASIER TO TARGET AND TREAT WITH GENE THERAPIES. SHOULDN'T TAXPAYER DOLLARS GO WHERE THERE'S A HIGHER CHANCE OF SUCCESS...

CHAIRMAN IMBASCIANI: CLAUDETTE, YOU PROBABLY SHOULD EXTEND HER TIME.

MS. FITTER: ...AND WE HAVE MORE OF A CHANCE TO BE INNOVATIVE WITH CLINICAL TRIAL DESIGN, WHICH IS A HUGE GOAL FOR CIRM. THANK YOU SO MUCH FOR HEARING US AND FOR YOUR PARTNERSHIP WITH OUR COMMUNITY.

MS. MANDAC: THANK YOU SO MUCH. LEAH.

DR. HOUSTON: I DON'T HAVE ANY COMMENTS. I'M HERE TO LEARN.

MS. MANDAC: ALL RIGHT. SO WE HAVE NEXT BRENDA.

DR. PORTER: I'M DR. BRENDA PORTER, AND THIS IS MY COLLEAGUE, DR. EMILY SPELBRINK. WE'RE BOTH PEDIATRIC NEUROLOGISTS AT STANFORD. I'M A PROFESSOR OF NEUROLOGY, AND I STUDY PEDIATRIC EPILEPSY. MY CLINICAL LOAD IS QUITE HIGH, AND I

HAVE A LARGE PATIENT POPULATION THAT HELPS DR. SPELBRINK WITH PEDIATRIC EPILEPSY. AND OUR PATIENT POPULATION IS REALLY LOTS OF PATIENTS WITH LOTS OF RARE DISEASES. SO WE BASICALLY TAKE CARE OF KIDS WITH TONS OF DIFFERENT DISORDERS THAT ARE GENERALLY PRETTY SEVERE.

AND THIS WAS FANTASTIC. I HAD NEVER BEEN TO ONE OF THESE CIRM MEETINGS. SO THANK YOU. REALLY INTERESTING WORK YOU GUYS ARE DOING.

ONE OF THE REASONS WE WANTED TO SPEAK WAS REALLY TO FOCUS ON THAT ISSUE THAT WE HAVE WHERE ALL OF OUR PATIENTS HAVE RARE DISEASES. AND WE HAVE DRUG COMPANIES COME TO US WITH THERAPIES, BUT THEY'RE NOT USUALLY TARGETING SUPER RARE DISEASES, BUT THAT'S THE MAJORITY OF THE PATIENTS WE HAVE. SO I THINK IT'S FANTASTIC THAT YOU'RE CONSIDERING CONTINUING IN THAT SPACE.

TWO THINGS I'D LIKE TO KIND OF POINT OUT WAS LONG AGO WHEN WE WOULD GET NIH FUNDING, WE ALL HAD OUR OWN IRB'S. AND THE NIH SAID, "NO. YOU'RE GOING TO USE A CENTRAL IRB." AND THAT WAS A HUGE HELP TO ALL OF US WHO WERE DOING TRIALS BECAUSE IT TOOK FOREVER FOR A LOCAL IRB TO APPROVE THINGS. AND SO ONCE THE FUNDING AGENCY SAID, "YOU ARE GOING TO USE A CENTRALIZED IRB," WE HAD MUCH BETTER SUCCESS

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

IN GETTING PATIENTS INTO TRIALS QUICKLY.

SO I THINK YOU'RE IN A GREAT POSITION IF YOU'RE FUNDING SOME OF THESE TRIALS IN RARE DISEASES TO REALLY THINK THROUGH WHAT YOU WANT OUR INSTITUTIONS TO GET OUT OF THE GRANTS AND WHAT YOU WANT THE PATIENTS TO GET OUT OF THE GRANTS AND HOW WE CAN INTERACT WITH COMPANIES. BECAUSE IN THIS RARE-DISEASE SPACE, JUST LIKE WAS MENTIONED, IT'S SUPER HARD TO GET COMPANIES INTERESTED IN THE DISORDERS, AND IT'S TRICKY FOR US TO WALK THE LINE BETWEEN STANFORD AND THESE RARE-DISEASE COMPANIES TO MAKE SURE THAT EVERYBODY IS BENEFITING, BUT YET MOVING FORWARD QUICKLY. SO IT WOULD BE FANTASTIC IF YOU GUYS CAN THINK THROUGH THAT A LITTLE BIT.

THE OTHER THING IS I HOPE THAT YOU'LL DO A COMBINATION OF FUNDING OF REALLY EARLY, RADICAL, NEW IDEAS ON HOW TO GENE THERAPIES INTO PATIENTS, BUT ALSO SORT OF LOOK AT THE CURRENT PIPELINE OUT THERE, SUCH AS AV 9S, WHICH ARE REALLY PROBABLY THE STANDARD RIGHT NOW, AND FUND BOTH. LIKE THINK ABOUT IT AS TRYING TO GET US TO THE FUTURE, BUT ALSO WHAT'S AVAILABLE NOW. SO THANK YOU. THIS WAS REALLY FANTASTIC.

CHAIRMAN FISCHER-COLBRIE: OKAY. CLAUDETTE, I DON'T THINK WE HAVE ANY OTHER PUBLIC

COMMENT.

DR. WEST: I DO. I DO.

CHAIRMAN FISCHER-COLBRIE: OKAY. SORRY.

DR. WEST: CAN YOU HEAR ME OKAY?

MS. MANDAC: YES, WE CAN HEAR YOU.

DR. WEST: ARE YOU ABLE TO HEAR?

MS. MANDAC: YES. CAN YOU HEAR US, JUSTIN?

DR. WEST: YEAH. CAN YOU HEAR ME OKAY?

MS. MANDAC: YES.

DR. WEST: ALL RIGHT. THANK YOU FOR THE OPPORTUNITY TO SPEAK AND FOR THE VITAL WORK YOU ARE DOING AT CIRM. MY NAME IS JUSTIN WEST. I WAS BORN, RAISED, AND PRACTICE MEDICINE IN CALIFORNIA. I COME BEFORE YOU TODAY AS A RARE-DISEASE ADVOCATE AND THE EXHAUSTED FATHER OF A SEVEN-YEAR-OLD BOY WITH AN ULTRA-RARE EPILEPSY. MY FAMILY JUST HASN'T BEEN TO THE BREAKING POINT. WE HAVE LIVE THERE EVERY SINGLE DAY, DEALING WITH THE DEVASTATION THAT COMES WITH WATCHING A YOUNG LIFE STOLEN, STRUGGLING TO KEEP A CHILD ALIVE WHO TRIES TO DIE EVERY MONTH, AND THE ALWAYS LOOMING FEAR OF WHAT HAPPENS IF HE OUTLIVES US.

WE'RE LIVING IN A GOLDEN AGE OF SCIENCE WHERE WE CAN IDENTIFY THE GENETIC CAUSE OF DISEASE

AND QUICKLY DEVELOP TREATMENTS TO ADDRESS THEM. SEVERAL RARE-DISEASE GROUPS HAVE ALREADY DONE THIS. SIMPLY PUT, THE REST OF US NEED FUNDING.

I BELIEVE A DISPROPORTIONATE AMOUNT OF THE CURRENT FUNDING IS ALLOCATED FOR DISEASES THAT ALREADY HAVE ADEQUATE TREATMENTS AND TO DISEASES THAT ARE SO COMPLEX THAT BILLIONS OF DOLLARS HAVE RESULTED IN NO CLINICALLY MEANINGFUL IMPACT. CONSIDER SOME OF THE CURRENT FUNDING.

FIFTY MILLION TO HIV CLINICAL TRIALS, YET HIV IS NOW A CHRONIC DISEASE WITH A LIFE EXPECTANCY SIMILAR TO THOSE WITHOUT THE INFECTION. A HUNDRED MILLION TO GLIOBLASTOMA RESEARCH, A DISEASE THAT HAS SEEN NO IMPROVEMENT IN FIVE-YEAR SURVIVAL RATES DESPITE BILLIONS OF DOLLARS SPENT OVER 30 YEARS.

ON A SLIDE EARLIER TODAY, TYPE 2 DIABETES WAS LISTED. I WOULD ALSO ARGUE AGAINST FUNDING TREATMENTS FOR DISEASES THAT ARE CAUSED BY AND TREATABLE WITH LIFESTYLE CHOICES. AS A FATHER OF A CHILD FACING A 50-PERCENT TEN-YEAR MORTALITY AND THE BROTHER OF A FOUR-YEAR-OLD WHOSE LIFE WAS CUT SHORT BY GLIOBLASTOMA, I ASK YOU TO CONSIDER THIS. REDUCE FUNDING FOR DISEASES WHERE THE MECHANISM IS UNCLEAR OR TREATMENT STRATEGIES AREN'T WELL DEFINED. STOP FUNDING PROGRAMS TO TREAT DISEASES THAT ALREADY HAVE

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

TREATMENTS. WE SEE LIMITED RESOURCES ALLOCATED TOWARD ULTRA-RARE DISEASES IN WHICH THE MECHANISM IS KNOWN, THE PATHWAY FOR GENE THERAPY IS CLEAR, AND THERE IS REAL POTENTIAL TO DEVELOP THERAPIES THAT CAN RESULT IN REDUCED SUFFERING AND MORTALITY. THE OPPORTUNITIES BEING MISSED ARE STAGGERING.

UNLIKE THE PREVALENT DISEASE COMMUNITY, A LACK OF FUNDING OPTIONS HAS FORCED FAMILIES TO TAKE MATTERS INTO THEIR OWN HANDS. WHETHER YOUR CHILD FACES CATASTROPHIC DISABILITY OR A DEATH SENTENCE, YOU DON'T HAVE THE LUXURY OF WAITING FOR PHARMA. INSTEAD, PARENTS LIKE ME QUIT JOBS, START FOUNDATIONS, ASSEMBLE ADVISORY BOARDS, OPEN PATIENT REGISTRIES, CONDUCT NATURAL HISTORY STUDIES, POPULATE BIOBANKS, GENERATE CELL LINES, AND ESTABLISH INTERNATIONAL RESEARCH COLLABORATIONS. WE BECOME THE UNTRAINED CEO'S OF THE ONLY COMPANY THAT TRULY MATTERS TO US WHERE FAILURE ISN'T MEASURED IN DOLLARS, BUT IN LIVES.

FOR SEVEN YEARS WE'VE CARED FOR ANDREW 24 HOURS A DAY, CHANGING DIAPERS, SPOON FEEDING EVERY MEAL, STARTING IV'S WHEN HE REFUSES TO DRINK, AND MEETING EVERY OTHER NEED FOR OUR FUNCTIONAL SIX-MONTH-OLD DAY IN AND DAY OUT. EVERY TIME ONE OF OUR OTHER CHILDREN HITS A MILESTONE, WE DIE A LITTLE

INSIDE KNOWING ANDREW WILL LIKELY NEVER EXPERIENCE THOSE MOMENTS. THIS IS OUR REALITY, BUT IT DOESN'T HAVE TO BE. SHIFT THE FUNDING STRATEGY FOR CIRM COULD BE LIFE CHANGING FOR PATIENTS LIKE ANDREW. OTHER GROUPS HAVE GONE FROM TREATMENT CONCEPT TO TRIAL IN LESS THAN TWO YEARS. THE REST OF THE ULTRA-RARE COMMUNITY IS DESPERATE FOR SUPPORT TO HAVE THEIR OWN CLINICAL TRIALS, TRIALS THAT COULD DRASTICALLY REDUCE PHYSICAL --

MS. MANDAC: THANK YOU SO MUCH. THAT IS IT FOR THE HANDS RAISED FOR PUBLIC COMMENT, MARK.

CHAIRMAN FISCHER-COLBRIE: OKAY. WITH THAT, THANK YOU FOR EVERYONE'S TIME. I VERY MUCH APPRECIATE THE PUBLIC COMMENTS WHICH ARE A VERY IMPORTANT PART OF THE OVERALL PROCESS AND DISCUSSION. AND I LOOK FORWARD FOR CONTINUING THE PROCESS HERE OF MARSHALING ALL THE ACTIVITY TO COME TO THE BEST GOAL THAT WE CAN POSSIBLY COME TO. SO LOOK FORWARD TO NEXT STEPS. AND, AGAIN, IN ADVANCE I VERY MUCH APPRECIATE EVERYONE'S EFFORTS DIRECTED TO DRIVING SOLUTIONS AS WE GO FORWARD. SO THANK YOU. WITH THAT, WE'RE ADJOURNED, RIGHT, SCOTT?

MR. TOCHER: THAT'S RIGHT. WE STAND ADJOURNED. THANK YOU, MARK.

VICE CHAIR BONNEVILLE: THANK YOU,

EVERYONE.

(THE MEETING WAS THEN CONCLUDED AT 1:23 P.M.)

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

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE VIRTUAL PROCEEDINGS BEFORE THE JOINT MEETING OF THE SCIENCE SUBCOMMITTEE AND THE 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 AUGUST 16, 2024, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CA CSR 7152
133 HENNA COURT
SANDPOINT, IDAHO
(208) 920-3543