BEFORE THE
SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS
WORKING GROUP
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: JANUARY 5, 2023
9 A.M.

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

THURSDAY, JANUARY 5, 2023; 9 A.M.

DR. LOMAX: YOU WANT TO KICK US OFF HERE, J.T. JEFF. APOLOGIES.

CO-CHAIRMAN KAHN: NO PROBLEM. GOOD MORNING. THOSE OF YOU ON THE WEST COAST AND GOOD AFTERNOON IF WE HAVE ANYBODY JOINING FROM EASTERN TIME ZONE. I'M JEFF KAHN. I AM IN MY PROFESSIONAL LIFE THE DIRECTOR OF THE BERMAN INSTITUTE OF BIOETHICS AT JOHNS HOPKINS UNIVERSITY. AND I'M PRIVILEGED TO BE THE CO-CHAIR, ALONG WITH MY COLLEAGUE FRED FISHER, OF THE CIRM STANDARDS WORKING GROUP. AND IT'S MY PRIVILEGE TO KICK OFF THE GAVEL TO OPENING THE JANUARY 2023 MEETING OF THE STANDARDS WORKING GROUP.

GEOFF, DO YOU WANT TO TAKE THE ROLL CALL OF THE MEMBERS AND I GUESS OF THE LEADERSHIP WHO ARE ALSO ON THE ZOOM.

DR. LOMAX: GREAT. YES. THANK YOU, JEFF, AND THANK YOU FOR ALL YOUR LEADERSHIP IN TERMS OF GETTING THIS MEETING TOGETHER. I'LL START WITH ROLL CALL. JEFFREY KAHN.

CO-CHAIRMAN KAHN: THAT'S ME. AS YOU HEARD, I'M AT JOHN HOPKINS UNIVERSITY. I WORK IN ETHICS AND PUBLIC HEALTH POLICY, DO A LOT OF WORK IN

ETHICS AND EMERGING TECHNOLOGIES AND, IMPORTANT FOR THIS ROLE, I'M A CALIFORNIA NATIVE. I GREW UP IN THE SAN FERNANDO VALLEY. PROUD GRADUATE OF GRANT HIGH SCHOOL AND UCLA. SO VERY HAPPY TO BE PART OF THIS GROUP AND TO CONTRIBUTE AS I CAN TO THE GREAT WORK OF CIRM.

DR. LOMAX: FRED FISHER.

CO-CHAIRMAN FISHER: HI, EVERYONE. AS YOU HEARD, I'M FRED FISHER, CO-CHAIR OF THIS WORKGROUP AND A MEMBER OF THE BOARD OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE. IN THAT ROLE, I AM THE PATIENT ADVOCATE FOR ALS AND MS AND SIT ON A NUMBER OF THE SCIENTIFIC REVIEW COMMITTEES PROVIDING GUIDANCE AND OVERSIGHT FOR THE HUNDREDS OF MILLIONS THAT CIRM INVESTS IN STEM CELL AND GENE THERAPY RESEARCH.

IN MY OTHER WORLD, I AM THE PRESIDENT AND CEO OF THE ALS ASSOCIATION GOLDEN WEST, WHICH SERVES PEOPLE THROUGHOUT CALIFORNIA AND HAWAII, PROVIDING DIRECT SUPPORT TO PEOPLE LIVING WITH ALS, WORKING WITH THE CLINICS AND INCUBATING CLINICS TO ENSURE THAT EVERYONE WITH ALS HAS ACCESS TO MULTIDISCIPLINARY SPECIALTY CARE, WORKING WITH RESEARCHERS TO HELP ACCELERATE THE SEARCH FOR EFFECTIVE TREATMENTS AND CURES FOR ALS, AND

ADVANCING PUBLIC POLICY INITIATIVES THAT ARE RELEVANT TO THE LIVES OF PEOPLE LIVING WITH ALS. I'VE BEEN IN THAT ROLE FOR JUST ABOUT 20 YEARS.

SO MY BACKGROUND IS IN SOCIAL WORK. SO I'M NOT A PHYSICIAN, I'M NOT A SCIENTIST, BUT CERTAINLY I CAN REPRESENT THE NEEDS, CONCERNS, AND PRIORITIES OF THE PATIENT COMMUNITY.

DR. LOMAX: AGAIN, JUST TO EXTEND A THANKS FOR ALL YOUR GUIDANCE IN TERMS OF PULLING THIS MEETING TOGETHER. FROM THE CIRM TEAM SIDE, IT'S DEEPLY APPRECIATED.

AKSHAY SHARMA.

DR. SHARMA: HI. GOOD MORNING, EVERYONE. I'M AKSHAY SHARMA. I'M A PHYSICIAN SCIENTIST. I'M A BONE MARROW TRANSPLANT PHYSICIAN AT ST. JUDE CHILDREN'S RESEARCH HOSPITAL. AND IN THIS ROLE I TAKE CARE OF CHILDREN WITH MANY DIFFERENT HEMATOLOGICAL DISORDERS, AND I ALSO LEAD CLINICAL TRIALS OF GENE THERAPY, GENE EDITING FOR SICKLE CELL DISEASE.

I'VE BEEN WORKING WITH CIRM FOR QUITE A FEW YEARS NOW IN DIFFERENT CAPACITIES. AND I'M HERE BECAUSE I'M ALSO AN ARMCHAIR ETHICIST, AS I TOLD JEFF KAHN PREVIOUSLY. MY INTEREST AS A PART OF MY RESEARCH ACTIVITIES ALSO REVOLVES AROUND EQUITABLE

PATIENT ACCESS AND DEVELOPING BETTER INFORMED CONSENT METHODS. I'M REALLY GLAD THAT CIRM IS LEADING THESE EFFORTS HERE AND HAPPY TO BE PART OF THIS.

DR. LOMAX: THANK YOU. BENHUR LEE.

DR. LEE: SORRY. I'M A PROFESSOR OF MICROBIOLOGY AT THE ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI. I WAS ACTUALLY INVOLVED IN THE ESCRO COMMITTEE AT UCLA EVER SINCE PROPOSITION 71 WAS APPROVED. BUT I MOVED TO SINAI AND I GUESS WAS DOING TOO GOOD A JOB AT THE ESCRO COMMITTEE AND WAS TO CONTINUE IN MY ROLE.

I'VE BEEN A MEMBER FOR THE LAST FEW YEARS AT THE RECOMBINANT DNA ADVISORY COMMITTEE AT NIH THAT HAS NOW BEEN RENAMED NEXTRAC TRACK, WHICH I GUESS IS NEW AND EXTRAORDINARY RESEARCH ADVISORY COMMITTEE. I THINK NIH IS MORE PROUD OF THE ACRONYM THAN THE COMMITTEE. BUT IN THAT CAPACITY, I HOPE TO LEARN AND CONTRIBUTE TO THE GREAT WORK THAT CIRM IS DOING. I'M MOSTLY A VIROLOGIST BY TRAINING.

DR. LOMAX: THANK YOU.

IS CHRISTINE MIASKOWSKI ON THE CALL? SO ONE OF OUR NURSE AND PATIENT ADVOCATE MEMBERS, BUT WASN'T ABLE TO JOIN TODAY.

ELENA FLOWERS.

DR. FLOWERS: HI, EVERYONE. THANK YOU FOR THE OPPORTUNITY TO BE HERE. IT'S WONDERFUL TO MEET ALL OF YOU. I AM ON THIS WORKING GROUP IN MY ROLE AS A NURSE AND PATIENT ADVOCATE ON THE BOARD FOR CIRM AND WAS REALLY HAPPY TO BE GIVEN THE OPPORTUNITY TO SERVE IN THAT CAPACITY, PARTICULARLY WITH THE FOCUS ON SERVING A DIVERSE PATIENT POPULATION OF CALIFORNIA. I LOVED AKSHAY'S COMMENT BEING AN CHAIR ARM ETHICIST AND LONG HAD AN INTEREST IN ETHICS AS WELL.

AND I'M AN ASSOCIATE PROFESSOR IN THE SCHOOL OF NURSING AT UC SAN FRANCISCO MOSTLY DOING RESEARCH FOCUSED ON MOLECULAR MARKERS RELATED TO RISK FOR TYPE 2 DIABETES AND LOOKING AT HOW WE CAN BETTER QUANTIFY SOCIAL DETERMINANTS OF HEALTH AND TEACH THE COURSES ON GENOMICS FOR OUR NURSING STUDENTS.

DR. LOMAX: THANK YOU.

HAD A MESSAGE FROM DR. ROSSANT. SHE'S NOT ABLE TO JOIN THIS MORNING.

DR. JOHN WAGNER.

DR. WAGNER: HI, EVERYONE. MY NAME IS JOHN WAGNER. I'M PREVIOUSLY THE DIRECTOR OF THE BONE MARROW TRANSPLANT CELL THERAPY PROGRAM AT THE UNIVERSITY OF MINNESOTA. NOW I'M THE DIRECTOR OF

THE INSTITUTE FOR CELL AND GENE IMMUNOTHERAPY AT THE SAME INSTITUTION. AND I'M PART OF THE GRANTS WORKING GROUP OF CIRM, BUT ALSO SERVED ON THE FIRST SWG WAY BACK IN MID-2000S WHERE THE FOCUS WAS HOW DO WE DO EMBRYONIC STEM CELL RESEARCH AND ALL THE DERIVED THERAPEUTICS FROM THAT.

YOU CAN IMAGINE THERE WERE MANY POLICY ISSUES TO DISCUSS IN THOSE EARLY DAYS. BUT MY INTEREST NOW CONTINUES TO BE FIRST-IN-HUMAN CELL AND STEM CELL AND IMMUNE CELL THERAPIES IN PATIENTS MOST OFTEN WITH GENETIC DISEASES OR CANCER.

DR. LOMAX: THANK YOU.

IS KAREN ROMMELFANGER ON THE CALL? I'M NOT -- OKAY. THAT'S A NO.

KAROL WATSON. CHRIS SAHA.

DR. SAHA: GOOD MORNING. I'M CHRIS SAHA FROM THE UNIVERSITY OF WISCONSIN MADISON. I'M AN ASSOCIATE PROFESSOR OF BIOMEDICAL ENGINEERING, AND I ALSO HOLD AN APPOINTMENT IN THE MEDICAL HISTORY AND BIOETHICS DEPARTMENT.

I RUN A LAB HERE ON DEVELOPING NEW CELL AND GENE THERAPIES, NOTABLY USING GENOME EDITING AND CRISPR. AND WE HAVE A NUMBER OF PROJECTS THAT ARE LOOKING TO MOVE EMERGING NEW TECHNOLOGIES HERE WITH GENOME EDITING INTO FIRST-IN-HUMAN TRIALS. I HAVE

ALSO BEEN PART OF THE STEM CELL RESEARCH OVERSIGHT COMMITTEE HERE AT UNIVERSITY OF WISCONSIN SINCE I STARTED FOR NEARLY TEN YEARS HERE. AND ALSO AM A MEMBER OF THE ETHICS COMMITTEE FOR THE INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH AS WELL AS THE AMERICAN SOCIETY FOR GENE AND CELL THERAPY.

PART OF MY TIME HAS BEEN TO ALSO CO-DIRECT A MULTI-INSTITUTIONAL EFFORT CALLED THE GLOBAL OBSERVATORY ON GENOME EDITING. AND I'VE BEEN VERY INTERESTED IN HOW THOSE TECHNOLOGIES ARE BEING INTEGRATED INTO BOTH RESEARCH AND TRANSLATIONAL WORK. THANK YOU FOR HAVING ME.

DR. LOMAX: LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: GOOD MORNING, EVERYONE. AND I APOLOGIZE I'M NOT ON CAMERA. I'M RECOVERING FROM SURGERY. I'M ALSO HAVING SOME PROBLEMS ACCESSING MY NORMAL LAPTOP AND DESKTOP. I THINK WHILE I WAS OUT ON MEDICAL LEAVE, MY DEVICES DECIDED THEY WERE OUT AS WELL AND THEY'VE NOT RETURNED.

BUT I'M DR. LEONDRA CLARK-HARVEY. I'M A PSYCHOLOGIST BY TRAINING AND HAVE PRACTICED IN COMMUNITY-BASED ORGANIZATIONS HERE IN CALIFORNIA AS WELL AS WISCONSIN. GO BADGERS. THANKS FOR THE FELLOW BADGER.

I AM THE CEO OF THE CALIFORNIA COUNCIL OF

COMMUNITY BEHAVIORAL HEALTH AGENCIES, AND WE REPRESENT MENTAL HEALTH AND SUBSTANCE USE DISORDER AGENCIES ACROSS THE STATE OF CALIFORNIA. I SIT ON THE BOARD OF THE NATIONAL COUNCIL FOR MENTAL WELL-BEING. REALLY GLAD TO BE HERE AMONGST THIS GROUP. THANK YOU.

DR. LOMAX: THANK YOU.

I KNOW MELISSA LOPES WAS NOT ABLE TO ATTEND THIS MEETING AS SHE WAS ON TRAVEL.

IS DR. RAYNE ROUCE ON THE CALL? AND I THINK THAT'S NO. AND THEN SHARON TERRY. OKAY. SO PERHAPS THEY WILL JOIN LATER.

THOSE ARE THE INTRODUCTIONS FOR THE APPOINTED MEMBERS TO THE STANDARDS WORKING GROUP. I KNOW WE HAVE A FEW PARTICIPANTS EITHER FROM OUR BOARD OR THE CIRM LEADERSHIP TEAM ON THE ZOOM. DR. MILLAN, WOULD YOU LIKE TO SAY AN INTRODUCTION?

DR. MILLAN: GOOD MORNING, EVERYBODY. I'M MARIA MILLAN, THE PRESIDENT AND CEO OF CIRM. I'VE BEEN HERE TEN YEARS, FIVE YEARS AS THE CEO. I HAD THE GREAT HONOR OF LEADING CIRM AT THE END OF THE PROP 71 ERA AND LAUNCHING INTO THIS CURRENT ERA UNDER PROP 14 WITH THE PASSAGE OF THE 2020 BOND INITIATIVE. AND SO WE ARE VERY EXCITED TO HAVE THIS GROUP TOGETHER BECAUSE THERE'S SOME VERY IMPORTANT

WORK AHEAD OF US.

WE'VE EXPANDED OUR CLINICAL TRIAL PORTFOLIO TO 86 CLINICAL TRIALS, WHICH IS TRULY REMARKABLE, AND IT'S CONTINUING TO EXPAND. AS YOU KNOW, THE ACCESS AND AFFORDABILITY AND EQUITY ASPECTS OF DELIVERING THESE TECHNOLOGIES AS WELL AS CLINICAL TRIALS AND THEN DOWNSTREAM ACCESS FOR THE COMMUNITIES IS A VERY IMPORTANT OBJECTIVE OF CIRM. SO THIS GROUP, WE'RE REALLY VERY FORTUNATE TO HAVE YOUR EXPERTISE DISCUSSING ALL THE ISSUES SURROUNDING THIS. THANK YOU SO MUCH.

DR. LOMAX: THANK YOU. MARIA BONNEVILLE.

MS. BONNEVILLE: HI THERE. I'M MARIA BONNEVILLE. I CURRENTLY AM THE VICE PRESIDENT OF PUBLIC OUTREACH AND BOARD GOVERNANCE. THAT TEAM IS TASKED WITH NOT ONLY BEING THE LIAISON WITH OUR 35-MEMBER BOARD, BUT ALSO COMMUNICATIONS AND OUTREACH TO COMMUNITIES THAT WE LIKE TO REACH IN CALIFORNIA OR TRY TO REACH IN CALIFORNIA. IF WE THINK ABOUT IT, THERE'S 40 MILLION PEOPLE. SO WE TRY AND HAVE DIFFERENT OUTLOOKS AND APPROACHES FOR DIFFERENT COMMUNITIES.

I WILL BE ASSUMING THE VICE CHAIR POSITION OF THE ICOC IN JANUARY, AND I LOOK FORWARD TO WORKING WITH THIS GROUP IN THE FUTURE. THANK YOU.

DR. LOMAX: I BELIEVE THE REMAINDER OF THE CIRM TEAM ON THE CALL WILL BE MAKING PRESENTATIONS. SO I'LL JUST ALLOW THEM TO INTRODUCE THEMSELVES AT THE BEGINNING OF THEIR PRESENTATION. AND I BELIEVE WE HAVE ONE ADDITIONAL BOARD MEMBER ON THE CALL. DR. GOLDSTEIN, WOULD YOU LIKE TO SAY A FEW WORDS?

DR. GOLDSTEIN: SURE. THANK YOU, JEFF. MY CAMERA IS OFF BECAUSE I'M ALSO FLAT ON MY COUCH RECOVERING FROM SURGERY. SO I APOLOGIZE FOR THAT.

I'M AT UC SAN DIEGO. I'M THE SANFORD CONSORTIUM FOR REGENERATIVE MEDICINE. AND HAVING RECENTLY READ THE HORRIFYING BOOK, *MEDICAL APARTHEID*, I'VE BECOME QUITE INTERESTED IN CONSENT ISSUES SINCE I THINK THAT'S ULTIMATELY THE POINT OF THAT BOOK. THANK YOU.

DR. LOMAX: THANK YOU.

I BELIEVE THAT COVERS THE INTENDED INTRODUCTIONS UNLESS I MISSED SOMEONE.

CO-CHAIRMAN KAHN: J.T.

DR. LOMAX: I WAS GOING TO TURN IT OVER TO J.T. ONE OTHER REMINDER. JUST SO EVERYONE IS AWARE, YOU GOT THE NOTICE, I THINK, ON THE ZOOM, BUT THIS MEETING IS BEING RECORDED, TRANSCRIBED, AND WILL REMAIN IN THE PUBLIC DOMAIN. SO JUST TO PROVIDE THAT DISCLOSURE. THANK YOU.

CO-CHAIRMAN KAHN: I'D JUST SAY ONE THING TOO. EVERYBODY IS BEHAVING THIS WAY ALREADY, BUT JUST TO REMIND FOLKS TO MUTE THEIR MICROPHONES WHEN THEY'RE NOT SPEAKING WILL HELP ON THE ZOOM. AND WE'LL USE THE HAND RAISE FUNCTIONS. I THINK WE'VE ALL GOTTEN SO USED TO THAT IN THE LAST THREE YEARS, WE KNOW HOW TO DO IT, BUT I THOUGHT I WOULD JUST SAY SO ANYWAY. GREAT.

CHAIRMAN THOMAS: JEFF, I WILL TAKE IT FROM HERE. THIS IS J.T., CHAIRMAN OF THE CIRM BOARD. I ALSO APOLOGIZE FOR BEING ON THE PHONE. I'M UNABLE TO GET ON MY INTERNET HERE IN LOS ANGELES THIS MORNING.

IT'S A GREAT PLEASURE TO WELCOME ALL OF YOU TO THIS VERY IMPORTANT MEETING OF THE STANDARDS WORKING GROUP. I, BY THE WAY, HAPPEN TO BE ALSO COINCIDENTALLY WITH CHAIRMAN KAHN A GRADUATE OF GRANT HIGH SCHOOL IN LOS ANGELES. SO IT'S ALWAYS NICE TO HAVE A HAVE A COUPLE OF LANCERS ON THE CALL WHEN YOU CAN.

I'VE HAD A GREAT DEAL OF INTEREST IN THE MEDICAL AND ETHICAL ISSUES SURROUNDING THE FIELD FOR MANY YEARS ACTUALLY GOING BACK BEFORE THERE WAS A STEM CELL FIELD THAT WE ALL ARE INVOLVED IN. I TAUGHT A COURSE IN LAW SCHOOL ON THE ETHICAL ISSUES

ARISING FROM GENETIC ENGINEERING AND MANIPULATION, THE TERMINOLOGY BACK IN THE DAY, AND HAVE BEEN MOST INTERESTED IN THE SUBJECT MATTER EVER SINCE.

THE LATEST PROPOSITION 14 THAT PASSED IN NOVEMBER OF '20 FOLLOWS THE IDEA OF PROP 71 IN CONVENING MEMBERS OF A STANDARDS WORKING GROUP TO DEAL WITH MEDICAL ISSUES AND ETHICAL STANDARDS THAT ARISE FROM OUR FIELD. AND THESE ARE MOST IMPORTANT. THEY CONTINUE TO CROP UP AS THE TECHNOLOGY ADVANCES AND SOMETHING THAT SERVES AS A GUIDANCE FOR CIRM AS WE CONTINUE ALONG THIS PROCESS OF FUNDING STEM CELL AND GENE THERAPY RESEARCH IN THE STATE OF CALIFORNIA.

SO THE ROLES THAT ALL OF YOU ARE PLAYING IN THIS CALL TODAY ARE CRUCIAL TO CIRM'S SUCCESS. AND I JUST WANTED TO THANK YOU ALL IN ADVANCE VERY MUCH FOR PARTICIPATING IN THIS, AND I LOOK FORWARD TO A ROBUST DISCUSSION ON THE MANY TOPICS ON THE AGENDA TODAY. THANK YOU VERY MUCH. GEOFF, BACK TO YOU.

DR. LOMAX: THANK YOU, J.T.

SO TO SET THE STAGE FOR THIS MEETING, WE'VE GOT A FEW, AS YOU CAN TELL FROM THE AGENDA, WE HAVE AN OVERVIEW OF THE MISSION OF THE WORKGROUP AND SOME BACKGROUND FROM OUR LEGAL TEAM ON THE BYLAWS

FOR THE WORKING GROUP. WE ARE HOPING WE CAN GET THAT COVERED AND THEN MOVE INTO SOME UPDATES ON SOME CIRM PROGRAM UPDATES. AND WE ANTICIPATE THAT WILL BE ABOUT THE FIRST THIRD OF THE MEETING, AND THEN WE'RE GOING TO TAKE A BREAK, A 30-MINUTE BREAK. SO JUST IN TERMS OF FOLKS THINKING ABOUT LUNCH, REFRESHMENTS, OR BREAKS, WE PROBABLY HOPEFULLY HAVE ABOUT AN HOUR AND A HALF TO TWO HOURS OF MATERIAL AND THEN WE'LL TAKE A HALF-HOUR BREAK. SO I JUST WANTED TO SET THE STAGE THERE AND LET YOU KNOW WHERE THE BREAK WAS.

MARIANNE, COULD WE GET THE SLIDES UP PLEASE, AND I'M GOING TO GO INTO AGENDA ITEM 2, WHICH IS WORKGROUP MISSION AND MEETING PURPOSE. IF YOU COULD -- THANKS. I THINK WE NEED TO SWITCH DISPLAYS. BEAUTIFUL. THANK YOU. AND THE NEXT SLIDE PLEASE.

SO OUR MISSION IS TO ACCELERATE WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO CALIFORNIA AND THE WORLD. NEXT SLIDE PLEASE.

THE AIM OF THIS PRESENTATION IS TO GIVE YOU AN OVERVIEW OF THE WORKING GROUP'S CHARGE AND HISTORY. AND THEN I WILL IDENTIFY SOME CONTEMPORARY

ETHICS POLICY TOPICS. NEXT SLIDE PLEASE.

SO THIS IS THE LANGUAGE FROM PROPOSITION 14. AND THIS REALLY SUMMARIZES THAT THE WORKING GROUP'S FUNDAMENTAL AIM IS TO PROVIDE OUR BOARD WITH RECOMMENDATIONS FOR STANDARDS ON BOTH THE CLINICAL ASPECTS OF OUR RESEARCH AND THE BASIC RESEARCH. AND IT SPANS EVERYTHING FROM SORT OF HUMAN SUBJECTS AND MEDICAL SIDE TO THE SOCIOECONOMIC AND FINANCIAL ASPECTS OF OUR RESEARCH AND INCLUDES CLINICAL TRIALS AND DELIVERY OF THERAPIES TO PATIENTS. NEXT SLIDE PLEASE.

THE GROUP IS COMPRISED OF FIVE PATIENT ADVOCATE MEMBERS OR NURSE MEMBERS FROM OUR BOARD, NINE SCIENTISTS AND CLINICIANS WITH EXPERTISE IN STEM CELL AND GENE THERAPY. YOU MAY NOTICE THAT CURRENTLY WE HAVE APPOINTED SIX OF THOSE NINE MEMBERS. SO WE'RE STILL IN THE PROCESS OF FILLING OUT THE WORKING GROUP. SO YOU RECEIVED THE ROSTER, YOU MAY NOTE THAT THE FOUR MEDICAL ETHICIST APPOINTMENTS HAVE BEEN MADE, AND THEY'RE, AGAIN, REFLECTED IN THE ROSTER, AND THE CHAIRPERSON OF THE ICOC, JON THOMAS. NEXT SLIDE PLEASE.

SO I'M GOING TO GIVE A VERY HIGH LEVEL SORT OF HISTORY OF SOME OF THE WORK THE GROUP HAS DONE MAINLY SO YOU GET A SENSE OF SORT OF THE RANGE

OF ISSUES WE'VE COVERED. AS DR. WAGNER ALLUDED TO, VERY EARLY ON THERE WAS A NEED FOR FOUNDATIONAL STANDARDS TO REALLY GUIDE THE BASIC ASPECTS OF STEM CELL RESEARCH AND SPECIFICALLY THE OVERSIGHT OF RESEARCH INVOLVING HUMAN EMBRYOS BECAUSE THERE WAS NO FEDERAL POLICY BECAUSE THAT RESEARCH IS NOT ALLOWED.

IN FACT, CIRM, UNDER PROPOSITION 71, ONE OF ITS INITIAL REASONS FOR BEING WAS TO ENABLE THAT RESEARCH WHICH OTHERWISE WAS NOT FUNDABLE BY NIH. HOWEVER, AT THAT TIME THE NATIONAL ACADEMIES OF SCIENCES DID PROVIDE A COMPREHENSIVE SET OF GUIDELINES TO GUIDE THAT WORK. AND CIRM ADOPTED THOSE GUIDELINES AND, IN FACT, PROPOSITION 14 DIRECTS CIRM TO REALLY MODEL STANDARDS AFTER THE NATIONAL ACADEMY. SO WE WERE ABLE TO ADOPT THOSE AND THEN FINALLY CODIFY THEM INTO FORMAL REGULATIONS THAT GUIDES CIRM-FUNDED RESEARCH AND WOULD ALLOW US TO ACTUALLY START FUNDING STUDIES.

SO THAT WAS THE EARLY PHASE WORK OF THE WORKING GROUP, REALLY PROVIDING GUIDANCE IN TERMS OF HOW TO STRUCTURE THOSE STANDARDS AND, AGAIN, SPECIFIC PROVISIONS FOR THE OVERSIGHT OF RESEARCH INVOLVING HUMAN EMBRYOS. NEXT SLIDE PLEASE.

SO FOLLOWING THE DEVELOPMENT OF OUR FORMAL

REGULATIONS, THERE WAS A NEED TO REALLY UNDERSTAND HOW THEY WERE WORKING AND HOW THEY COULD BE IMPROVED. SORT OF A BODY OF REGULATION ALWAYS SOUNDS GOOD CONCEPTUALLY, BUT THEN YOU HAVE TO GO OUT AND SEE HOW IT'S WORKING IN THE FIELD. SO WE SPENT ABOUT THREE YEARS DOING ON-SITE COMPLIANCE EVALUATIONS. WE HAD A SERIES OF WORKSHOPS WITH THE OFFICIALS FROM THESE INSTITUTIONS THAT WERE RESPONSIBLE FOR IMPLEMENTING THE GUIDELINES. AS DR. LEE ALLUDED TO, WE WORKED CLOSELY WITH THE ESCRO COMMITTEES TO REALLY UNDERSTAND HOW TO MAKE THESE RULES WORK IN A WAY THAT WAS CLEAR, TRANSPARENT, AND REALLY ACHIEVING THEIR PURPOSE OF EFFECTIVE OVERSIGHT.

AND WE CONTINUED TO INTERACT WITH THE NATIONAL ACADEMIES' EMBRYONIC STEM CELL RESEARCH OVERSIGHT COMMITTEE. THEY AMENDED THEIR GUIDELINES THREE TIMES, I BELIEVE, BETWEEN 2005 AND 2010. SO IT WAS WHAT I'D CHARACTERIZE AS A REFINEMENT STAGE OF REALLY GETTING THE POLICY TO BE EFFECTIVE AND ROBUST. NEXT SLIDE PLEASE.

AND THEN THE LAST SORT OF MAJOR PRODUCT OF THE WORKING GROUP WAS A MODEL CONSENT FORM FOR A LARGE INDUCED PLURIPOTENT STEM CELL BANK THAT CIRM WAS FUNDING. WE HAD A NUMBER OF MEETINGS AND

REPORTS TO DEVELOP A TEMPLATE THAT WOULD BE ULTIMATELY UTILIZED IN SEVEN LARGE-SCALE TISSUE COLLECTION AWARDS. AND THIS TEMPLATE WAS DESIGNED TO REALLY CAPTURE ALL THE SORT OF CONSENT AND DISCLOSURE-RELATED PROVISIONS THAT WOULD REALLY BE NECESSARY TO MAINTAIN A ROBUST IPS BANK WHERE STEM CELL LINES AND DONOR GENETIC DATA WOULD BE DISTRIBUTED BROADLY, NOT ONLY NATIONALLY, BUT INTERNATIONALLY.

AND TO THIS DATE OUR TEMPLATE CONTINUES TO BE RECOGNIZED AS ROBUST, AND THESE LINES HAVE BEEN UTILIZED INTERNATIONALLY FOR RESEARCH AND THEY CONTINUE TO DO SO. SO WE ARE QUITE PROUD OF THAT.

I'LL PAUSE THERE BEFORE GOING ON TO THE NEXT SLIDE JUST TO SEE IF THERE ARE ANY QUESTIONS, CLARIFICATIONS THAT ANYONE HAS. I'M NOT SEEING ANY HANDS. SO I WILL -- THANK YOU, JEFF. I WILL MOVE ON TO THE NEXT SLIDE.

SO IN TERMS OF MOVING FORWARD, AND WE'LL COME BACK, THE AIM IS TO SORT OF COME BACK TO A SLIDE LIKE THIS AT THE END OF THE DAY TO GET YOUR FEEDBACK. BUT THESE ARE THE TOPICS THAT WE CONTINUE TO TRACK AS WE RECOGNIZE THEY ARE ONGOING ISSUES THAT IMPACT BOTH THE RESEARCH WE FUND AND THE STANDARDS WE PROMULGATE TO GUIDE THAT RESEARCH.

THERE'S THE ONGOING HUMAN GENOME EDITING INITIATIVE WHICH IS BEING LED BY THE NATIONAL ACADEMIES. THERE HAVE BEEN REPORTS AND CONTINUE TO BE DISCUSSIONS ABOUT EMBRYO MODEL SYSTEMS AND TO WHAT EXTENT THERE'S ADDITIONAL OVERSIGHT OR REVIEW NECESSARY FOR THOSE TYPES OF STUDIES.

THERE'S HUMAN NEURAL ORGANOIDS AND THE GENERAL USE OF STEM CELL MODELING BOTH IN ANIMALS AND ULTIMATELY THE CLINICAL USE OF NEURAL STEM CELLS WHICH IS A TOPIC OF DISCUSSION.

BLASTOCYST COMPLEMENTATION STUDIES WHICH TENDS TO CENTER AROUND TO THE EXTENT THAT STEM CELLS CAN BE USED TO DEVELOP ORGANS IN ANIMALS WHICH MIGHT BE SUITABLE FOR HUMAN TRANSPLANTATION.

AND A TOPIC THAT CONTINUES TO CHALLENGE US IN THE FIELD ARE UNAUTHORIZED TREATMENTS OR STEM CELL CLINICS THAT ARE PROMOTING TREATMENTS THAT ARE USING STEM CELLS, BUT THOSE TREATMENTS HAVE NOT BEEN DEMONSTRATED TO BE SAFE AND EFFECTIVE. SO THESE ARE TOPICS THAT, AGAIN, WE'D LIKE TO COME BACK AT THE END OF THE DAY TO GET YOUR INPUT IN TERMS OF YOUR THOUGHTS ON BOTH AN EXTENSION OF THIS LIST AND OTHER TOPICS WE MIGHT WANT TO CONSIDER AS WE MOVE ALONG AS A WORKING GROUP.

SO I'LL PAUSE HERE. THIS IS MY LAST SLIDE

BEFORE WE GO ON TO THE NEXT PRESENTATION. BUT AGAIN, TAKE A MOMENT IF THERE'S QUESTIONS OR COMMENTS.

CO-CHAIRMAN KAHN: DON'T SEE ANY HANDS. THANK YOU FOR THAT VERY CLEAR PRESENTATION.

DR. LOMAX: SO WHY DON'T WE THEN MOVE ON. BEN, DO YOU WANT TO INTRODUCE YOURSELF. SORRY. I DID HAVE ONE MORE SLIDE. MY MISTAKE.

SO I DID WANT TO POINT OUT ONE OTHER ASPECT OF OUR WORK, REALLY CIRM'S WORK. WE HAVE THE BENEFIT OF SORT OF TREMENDOUS BRAIN POWER, IF YOU WILL, WITHIN THE CIRM SYSTEM. AND IN PARTICULAR, I WANTED TO POINT OUT THAT THE STANDARDS WORKING GROUP, THE WORK OF THIS WORKING GROUP REALLY INTERACTS WITH TWO OTHER WORKING GROUPS QUITE DIRECTLY. ONE IS OUR ACCESS AND AFFORDABILITY WORKING GROUP, WHICH IS FOCUSED ON ACCESS TO TRIALS AND TREATMENTS. AND YOU'RE GOING TO HEAR A PRESENTATION LATER THIS MORNING ABOUT THAT WORK. SO I WON'T SAY MUCH MORE THAN THAT.

AND THEN OUR GRANTS WORKING GROUP, WHICH, AS YOU'VE HEARD AGAIN THIS MORNING, A NUMBER OF THE MEMBERS ON THIS PANEL ALSO SERVE ON OUR GRANTS WORKING GROUP. AND WHAT'S IMPORTANT THERE IS THE GRANTS WORKING GROUP REALLY ENSURES A LEVEL OF

SCIENTIFIC EXCELLENCE IN TERMS OF OUR WORK. SO REALLY THE RECOGNITION THAT THE WORK WE ARE FUNDING HAS GONE UNDER RIGOROUS INDEPENDENT PEER REVIEW. I THINK FROM AN ETHICS STANDPOINT, THAT'S EXTREMELY IMPORTANT, THAT THE WORK THAT'S MOVING FORWARD HAS BEEN EVALUATED AND DEEMED SCIENTIFICALLY MERITORIOUS.

SO I WANTED TO PROVIDE THAT CONTEXT AS WELL SO THAT WE SEE HOW IN THE CIRM SYSTEM THE WORK OF THIS GROUP WILL INTERACT WITH THESE OTHER IMPORTANT WORKING GROUPS AND OTHER CIRM PROGRAMS. BUT THESE ARE THREE THAT -- THESE ARE TWO THAT ARE VERY IMPORTANT. THANK YOU. AND I THINK THAT'S MY LAST SLIDE. YES.

MR. HUANG: HELLO. GOOD MORNING. MY NAME IS BEN HUANG. I'M THE ASSOCIATE GENERAL COUNSEL AT CIRM. AND I'M HERE TO -- NEXT SLIDE PLEASE. I'M HERE TO JUST DO A VERY BRIEF PRESENTATION ON THE STANDARDS WORKING GROUP BYLAWS AND ALSO NON-ICOC CONFLICT OF INTEREST WHICH RELATES TO DISCLOSURE REQUIREMENTS.

AND I REALIZE THAT WE HAVE NOT EXPLAINED CIRM TERMINOLOGY HERE. SO REALLY QUICKLY, ICOC IS THE SHORTHAND FOR CIRM'S INDEPENDENT CITIZENS OVERSIGHT COMMITTEE, WHICH WE ALSO CALL OUR

GOVERNING BOARD. AND SO THE NON-ICOC CONFLICT OF INTEREST IS FAIRLY SPECIFIC TO A SUBSET OF THE STANDARDS WORKING GROUP MEMBERS, AND THE ICOC MEMBERS HAVE A MORE EXTENSIVE CONFLICT OF INTEREST DISCLOSURE REQUIREMENT. NEXT SLIDE PLEASE.

SO THE DUTIES OF THE STANDARDS WORKING GROUP ACTUALLY INCLUDES THE FOLLOWING IN OUR REGULATIONS. I BELIEVE GEOFF IN HIS EARLIER PRESENTATION CUT OVER A SECTION THAT IS KIND OF ENCAPSULATED IN B. BUT THIS IS THE OFFICIAL LIST, THE LEGAL LIST THAT'S IN OUR REGULATIONS. AND SO I WILL DO SOME READING HERE.

SO FOR A, THE SWG SHOULD RECOMMEND TO THE ICOC SCIENTIFIC AND MEDICAL ETHICAL STANDARDS AND MODIFICATIONS TO EXISTING STANDARDS.

B WE KIND OF COVERED, BUT I'LL JUST READ THIS OFF REALLY QUICKLY. RECOMMEND TO THE ICOC STANDARDS FOR ALL MEDICAL, SOCIOECONOMIC, DIVERSITY, AND FINANCIAL ASPECTS OF CLINICAL TRIALS AND THERAPY DEVELOPMENT AND DELIVERY TO PATIENTS. THIS MAY INCLUDE STANDARDS FOR EQUITABLE ACCESS TO THERAPIES, SAFE AND ETHICAL PROCEDURES FOR OBTAINING MATERIALS AND CELLS FOR RESEARCH, CLINICAL EFFORTS FOR THE APPROPRIATE TREATMENT OF HUMAN SUBJECTS, AND COMPLIANCE WITH PATIENT PRIVACY LAWS.

C IS MAKE RECOMMENDATIONS TO THE ICOC ON THE OVERSIGHT OF FUNDED RESEARCH TO ENSURE COMPLIANCE WITH THE STANDARDS ABOVE.

AND D IS REGULARLY ADVISE THE ICOC AND OTHER CIRM WORKING GROUPS ON RELEVANT ETHICAL AND REGULATORY ISSUES. NEXT SLIDE PLEASE.

THE STANDARDS WORKING GROUP BYLAWS SPECIFIES THE CO-CHAIR REQUIREMENTS. AND SO THE ICOC SHALL APPOINT A PATIENT ADVOCATE MEMBER OF THE SWG TO SERVE AS CO-CHAIR, AND THAT REPRESENTATIVE IS MR. FISHER. AND IN ADDITION, THE ICOC SHALL APPOINT A SCIENTIST CLINICIAN MEMBER OR AN ETHICIST MEMBER OF THE SWG TO SERVE AS CO-CHAIR, WHICH IS OBVIOUSLY DR. KAHN. NEXT SLIDE PLEASE.

THE SWG SHALL MEET IN PUBLIC SESSION, SUCH AS THE ONE TODAY, EXCEPT FOR DISCUSSIONS RELATED TO MATTERS INVOLVING PATIENT PRIVACY OR REVIEW OF A COMPLAINT REGARDING INVESTIGATORS' OR INSTITUTION'S COMPLIANCE WITH MEDICAL OR ETHICAL STANDARDS ADOPTED BY THE ICOC. AND ALSO DISCUSSION OF OTHER MATTERS THAT MAY BE CONSIDERED IN CLOSED SESSION UNDER STATE LAW. NEXT SLIDE.

FOR QUORUM, 65 PERCENT OF THE SWG MEMBERS WHO ARE ELIGIBLE TO VOTE SHALL CONSTITUTE A QUORUM. ALL ACTIONS OF THE SWG SHALL BE TAKEN BY A MAJORITY

VOTE OF THE QUORUM OF MEMBERS.

AND I THINK THAT'S JUST -- THE BYLAWS ARE ACTUALLY QUITE SHORT. SO THAT ENCAPSULATES THE BYLAWS.

THE MEMBERSHIP IS ALSO SPECIFIED. I'D LIKE TO NOTE THAT GEOFF COVERED THAT IN HIS PREVIOUS PRESENTATION, THE BREAKDOWN OF THE MEMBERSHIP FOR THE SWG. ARE THERE ANY QUESTIONS? OKAY. I WILL MOVE ON HERE TO CONFLICT OF INTEREST.

LIKE I NOTED EARLIER, THE CIRM ICOC MEMBERS HAVE MORE EXTENSIVE DISCLOSURE REQUIREMENTS THAN THOSE BELOW FOR THE NON-ICOC MEMBERS. A GENERAL POINT IN OUR CIRM CONFLICT OF INTEREST POLICY IS THAT THE NON-ICOC MEMBERS OF THE STANDARDS WORKING GROUP ARE PRECLUDED FROM DERIVING DIRECT FINANCIAL BENEFIT FROM CIRM THROUGH GRANTS, LOANS, OR CONTRACTS AND FROM ACTING AS A PRINCIPAL INVESTIGATOR ON ANY CIRM-FUNDED AWARD.

AND A CONFLICT OF INTEREST EXISTS WHEN THERE IS A FINANCIAL OR OTHER INTEREST THAT SIGNIFICANTLY IMPAIRS THE INDIVIDUAL'S OBJECTIVITY OR THAT CREATES AN UNFAIR ADVANTAGE FOR ANY PERSON, INSTITUTION, OR COMPANY. A NON-ICOC MEMBER HAS A CONFLICT OF INTEREST WHEN ANY FINANCIAL INTEREST IDENTIFIED IN SUBDIVISION B OF THIS PARTICULAR

REGULATION IS THE SUBJECT OF A DECISION BEFORE THIS WORKING GROUP. AND THE NEXT SLIDE CONTAINS ALL THE PROVISIONS OF THAT SUBDIVISION B. SO NEXT SLIDE PLEASE.

AND SO THIS IS THE DISCLOSURE WHICH SWG MEMBERS WILL PROVIDE TO CIRM, AND WE WOULD COMPARE THAT TO ANY ISSUES ON THE AGENDA THAT WILL BE THE SUBJECT OF A DECISION. SO FOR NON-ICOC MEMBERS, THEY MUST DISCLOSE THE FOLLOWING. IT IS CONFIDENTIAL. ALL CALIFORNIA-BASED ACADEMIC OR NONPROFIT RESEARCH INSTITUTIONS FROM WHICH THE STANDARDS WORKING GROUP MEMBERS, SPOUSES, OR BASICALLY OTHER FAMILY MEMBERS RECEIVE CURRENT INCOME OF $5,000 OR MORE. AND TWO WOULD BE ALL BIOTECH AND PHARMA COMPANIES FROM WHICH MEMBERS, SPOUSES, OR OTHER MEMBERS FROM WHOM A MEMBER HAS A COMMON FINANCIAL INTEREST RECEIVE CURRENT INCOME OR OTHER BENEFIT OF $5,000 OR MORE. AND THE LAST ONE IS ALL REAL PROPERTY INTEREST IN CALIFORNIA OF $5,000 OR MORE, INCLUDING REAL ESTATE INTERESTS OR INTERESTS IN IP, SUCH AS PATENTS OR COPYRIGHTS HELD BY MEMBERS, THEIR SPOUSES, OR OTHERS FROM WHOM A MEMBER HAS A COMMON FINANCIAL INTEREST.

AND SO CIRM WOULD COLLECT THIS INFORMATION. IT IS CONFIDENTIAL. AND WE WOULD

DETERMINE CONFLICTS PRIOR TO ANY DECISION-MAKING MADE BY THIS WORKING GROUP. AND THAT IS -- THOSE ARE BASICALLY THE ISSUES, I THINK, THAT APPLY TO THE STANDARDS WORKING GROUP, THE BYLAWS AND THE CONFLICT OF INTEREST. SO ARE THERE ANY QUESTIONS? OTHERWISE I THINK I PASS IT ON BACK TO YOU, GEOFF.

DR. LOMAX: SURE. ONE QUICK QUESTION, BEN. I BELIEVE WE ARE REVISING OUR DISCLOSURE FORM; IS THAT CORRECT? SO I JUST WANTED TO GIVE PEOPLE AN EXPECTATION THAT WE'LL BE RECIRCULATING THE DISCLOSURE FORM.

MR. HUANG: YES. WE'LL BE RECIRCULATING THE DISCLOSURE FORM. THANK YOU.

DR. LOMAX: OKAY. SO WE'RE GOING TO MOVE ON TO WHAT WE ARE CALLING THE CIRM PROGRAM UPDATES PART OF THE AGENDA. IT'S A SHOULD REALLY SAY SELECTED PROGRAM UPDATES. WHAT WE ARE REALLY KEYING IN ON ARE PROGRAM AREAS THAT IMPACT PATIENTS AND THE DELIVERY OF CELL AND GENE THERAPIES. AND SO WE WANTED TO REALLY GIVE YOU ALL A SENSE OF THE SCOPE OF CIRM CAPACITY AND INFRASTRUCTURE THAT GOES INTO THE DELIVERY OF SPECIFICALLY CLINICAL TRIALS.

SO WITH THAT, I WOULD LIKE TO INVITE DR. ABLA CREASEY TO INTRODUCE HERSELF AND BEGIN WITH AN OVERVIEW OF OUR CLINICAL TRIALS PORTFOLIO.

DR. CREASEY: THANK YOU, GEOFF. GOOD MORNING, EVERYONE. I AM ABLA CREASEY, AND I'M THE HEAD OF THERAPEUTICS DEVELOPMENT AT CIRM. I'M GOING TO GIVE YOU TODAY A BRIEF OVERVIEW OF OUR ACTIVE CLINICAL TRIAL PORTFOLIO THAT COVERS IND-ENABLING STUDY GRANTS AS WELL AS GRANTS THAT FILED AN IND WITH THE FDA AND HAVE APPLIED TO CIRM FOR FUNDING TO CONDUCT CLINICAL TRIAL RESEARCH STUDIES AND THAT HAVE BEEN CLEARED BY THE FDA. ALL THE PROTOCOLS WOULD HAVE BEEN GUIDED BY THE FDA AS WELL.

WE ALWAYS START OUR PRESENTATIONS WITH OUR MISSION. YOU'VE ALREADY HEARD IT FROM GEOFF, BUT I'M GOING TO SAY IT AGAIN. THE CIRM MISSION IS ACCELERATING WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO A DIVERSE CALIFORNIA AND WORLD. WE ACTUALLY LIVE BY THAT HOW WE PERFORM EVERY DAY'S WORK.

AS YOU KNOW, THE CIRM FUNDS SUPPORT THE PROVEN FUNDING MODEL IN FIVE KEY AREAS. ONE IS BASIC RESEARCH, WHICH IS WE CALL DISCOVERY, TRANSLATION, CLINICAL, INFRASTRUCTURE, AND EDUCATION. MY TEAM AND I WORK IN THE AREA OF TRANSLATION AND CLINICAL.

SO THE NEW STRATEGIC PLAN IS DESIGNED TO

ENHANCE, ORGANIZE, AND INTERCONNECT CIRM'S PROVEN FUNDING MODEL TO ACHIEVE THE OVERARCHING GOALS.

THE FIVE-YEAR STRATEGIC PLAN DISPLAYED ON THIS SLIDE INCLUDES THREE PRINCIPLES WITH SPECIFIC GOALS TO ACHIEVE FOR EACH. ONE IS ADVANCING FIRST-CLASS SCIENCE. SECOND IS DELIVER WORLD-CLASS SOLUTIONS. AND THIRD PROVIDE OPPORTUNITY FOR ALL.

FOR TODAY'S DISCUSSION I'M GOING TO CONCENTRATE ON A KEY COMPONENT OF THE FIVE-YEAR STRATEGIC PLAN, WHICH IS DELIVER REAL-WORLD SOLUTIONS -- THAT INCLUDES ADVANCING THERAPIES TO MARKETING APPROVAL -- AND MAINLY GIVE YOU A VIEW OF WHAT OUR CURRENT ACTIVE CLINICAL PORTFOLIO LOOKS LIKE. WE DON'T GENERALLY DO THAT. WE ACTUALLY HAVE A VERY NICE DATABASE ON OUR WEBSITE, AND EVERYONE IS WELCOME TO VIEW THAT AS WELL AT YOUR LEISURE.

SO THE THERAPEUTICS DEVELOPMENT TEAM, ALONG WITH COLLABORATION WITH SEVERAL OTHER GROUPS WITHIN CIRM, WE WORK CLOSELY TO MANAGE TRANSLATION AND CLINICAL GRANTS. CIRM HAS BEEN SUCCESSFUL IN ATTRACTING AND DERISKING PROJECTS IN EARLY STAGES, PREPARING FOR A PRE-IND MEETING. AND THAT'S THE END RESULT OF HAVING A TRANSLATION GRANT. CONDUCTING IND-ENABLING STUDIES, AND THAT'S WHAT A CLIN1 GRANT DOES. AND THEN PROGRESSING TO EARLY CLINICAL

DEVELOPMENT WITH SOME PROGRESSING TO MID TO LATE CLINICAL DEVELOPMENT, WHICH I WILL COVER LATER IN THE PRESENTATION.

AS YOU SEE IN THIS SLIDE, MUCH OF THE PORTFOLIO IS CURRENTLY IN THREE MAIN THERAPEUTIC AREAS: NEURO, ONCOLOGY, WHICH COVERS BLOOD AND SOLID CANCER, HEMATOLOGICAL DISORDERS SUCH AS SICKLE CELL AND THALASSEMIA. PLEASE NOTE THAT OUR PORTFOLIO IS A BY-PRODUCT OF A PASSIVE AND SOMEWHAT PROACTIVE PROCESS OF GRANTS SUBMISSION. THE TEAM AND BUSINESS DEVELOPMENT AS WELL AS OTHER GROUPS REACH OUT TO ACADEMIC AND NONPROFIT ORGANIZATIONS AND ENCOURAGE THEM TO APPLY TO CIRM. AND WE FREQUENTLY ADVISE AND CONSULT FOR THOSE WHO APPLY BEFORE THEY SUBMIT THE GRANT TO CIRM. AND, AGAIN, I WANT TO EMPHASIZE THAT MOST OF OUR GRANTS ARE IN EARLY DEVELOPMENT. SOME HAVE PROGRESSED TO MID-CLINICAL AND SOME PIVOTAL TO LATE CLINICAL, AND I'LL DESCRIBE THAT FURTHER LATER.

THE CLINICAL PORTFOLIO INCLUDES CLIN1 GRANTS, WHICH I SAID ARE FOR IND-ENABLING STUDIES. AND THEN THE CLIN2 GRANTS AFTER AN IND HAS BEEN FILED. I WANT TO ALSO EMPHASIZE THAT THE CLINICAL PROTOCOL HAD BEEN CLEARED BY THE FDA AND SHARED WITH US AFTER IT HAD DISCUSSION WITH THE REGULATORS. AS

YOU CAN SEE, THE PORTFOLIO CONTINUES TO COVER ALL STAGES OF CLINICAL DEVELOPMENT FROM IND-ENABLING TO PHASE 1, PHASE 1-2, PHASE 2, PHASE 3. AND THERE'S A SMALL NUMBER OF THE GRANTS IN LATE STAGE OF DEVELOPMENT, WHICH THE COLOR LIGHT BLUE AT THE END OF EACH OF THE BAR GRAPHS IS THOSE LATER STAGE GRANTS.

THE GRADUAL GROWTH OF THE CLINICAL TRIAL PORTFOLIO IS SHOWN ON THIS SLIDE. YOU HEARD DR. MILLAN MENTION THAT WE'VE SUCCESSFULLY BEEN ABLE TO RECRUIT 86 CLINICAL TRIALS. AND THAT'S BEEN QUITE AN ACHIEVEMENT BY EVERYONE. THAT ALL STARTED IN 2004 TO 2016. THERE WERE 17 GRANTS AWARDED, CLINICAL GRANTS AWARDED. AND BY THE END OF 2020, WE ACTUALLY ACHIEVED 51 NEW CLINICAL TRIALS, WHICH WAS ALSO AN ACHIEVEMENT THAT WAS NOT ACTUALLY PREDICTED. AND NOW WE ARE AT 86. SO ON OUR TRAJECTORY TO CONTINUE TO GO HIGHER AND HIGHER OVER TIME.

THE CLINICAL TRIALS COVER SEVERAL THERAPEUTIC AREAS IN VARIOUS DEVELOPMENT PHASES WHICH, AGAIN, I'LL SHARE WITH YOU MORE DETAILS. WHAT'S EXCITING IS THAT OVER 50 PERCENT OF THE CIRM-FUNDED CLINICAL PROJECTS ARE REALLY PARTNERED WITH INDUSTRY. AND THAT'S QUITE AN ACHIEVEMENT FOR BOTH THE GRANTEE AND CIRM.

THE THREE MOST PROMINENT THERAPEUTIC MODALITIES THAT ARE IN OUR DATABASE ARE GENE-MODIFIED CELL THERAPEUTICS, SUCH AS HSC'S AND MSC'S. AND THEN WE HAVE BIOLOGIC THERAPEUTICS THAT INCLUDE MONOCLONAL ANTIBODIES, BUT THE CAVEAT IS THAT THOSE ANTIBODIES HAVE TO HAVE A STEM CELL INVOLVEMENT. JUST WANTED TO NOTE THAT GENE THERAPY AS A FUNDED MODALITY WAS APPROVED BY THE ICOC, WHICH WE ALSO CALL THE CIRM BOARD, ONLY A COUPLE OF YEARS AGO. WE ARE STARTING TO SEE MORE AND MORE GENE THERAPY GRANT SUBMISSIONS. AND UP TO THIS EXAMPLE, WE WILL HAVE MORE IN THAT AREA IN THE NEXT COUPLE YEARS.

SO I'LL START IN MORE DETAILS, AND WE'LL GO THROUGH THIS QUICKLY, TO SHOW YOU THE DISTRIBUTION OF OUR ACTIVE CLINICAL TRIALS GRANTS THROUGH THE PHASES OF DEVELOPMENT WHICH YOU CAN SEE AND REVIEW ON THE CIRM WEBSITE AS I MENTIONED.

SO WHEN IT COMES TO ACTIVE PHASE 1 CLINICAL TRIALS, THERE ARE CURRENTLY 30 OF THEM. THERE ARE 15 DISPLAYED ON THIS SLIDE, AND I WILL SHOW YOU THE NEXT SLIDE TO COVER THE REST OF THE 30. BEFORE I DO THAT, I JUST WANTED TO MENTION THAT, IF YOU LOOK AT THE TARGET ENROLLMENT, YOU NOTICE THAT MOST OF THE TRIALS HAVE RELATIVELY SMALL NUMBER OF

PATIENTS. AND THAT ACCENTUATES THE FACT THAT IN PHASE 1 WE REALLY ARE EVALUATING THE SAFETY OF THE APPROACH. AND IT IS OFTEN, SINCE THIS IS CLINICAL RESEARCH, IT'S AN OPPORTUNITY FOR FOLKS TO LEARN MORE ABOUT THE MODALITY THEY'RE STUDYING AND ADJUST THEIR CLINICAL PROTOCOLS ACCORDINGLY.

SO HERE IS THE NEXT 15 PHASE 1 TRIALS. AGAIN, THE INDICATIONS VARY. I ALREADY MENTIONED NEUROLOGY, ONCOLOGY, AND HEMATOLOGICAL INDICATIONS TEND TO BE MORE PROMINENT.

AGAIN, DIVERSITY OF THE THERAPEUTIC AREAS IS INDICATED AGAIN IN THE PHASE 1 TRIALS; BUT, AGAIN, REMINDING YOU THAT WE ACCEPT EVERY GRANT THAT'S SUBMITTED PENDING THE GWG, THE GRANTS WORKING GROUP, RECOMMENDATION AND THEN ICOC APPROVAL. SO IT'S NOT UP TO THE CIRM RECRUITERS OR EMPLOYEES TO DO THAT PART, MEANING MY TEAM OR OTHER TEAMS OUTSIDE THE GWG AND ICOC.

SO WE HAVE THEN 12 PHASE 1-2 ACTIVE TRIALS. AND THE DISTINCTION OF THOSE IS THAT THE GRANTEES HAVE WORKED OUT A PROTOCOL IN WHICH THEY WILL RUN A PHASE 1 TRIAL TO ASSESS SAFETY ALONG WITH EVALUATING PRELIMINARY EFFICACY OF THEIR MODALITY. AND THAT'S, AGAIN, IN AGREEMENT WITH THE REGULATORS. AND FOR THAT REASON, WE ALSO DISTINGUISH PHASE 1

TRIALS ALONE.

AGAIN, IF YOU LOOK AT THE LAST COLUMN OF THE SLIDE, THE TARGETED ENROLLMENT IS MORE OR LESS SMALLER NUMBERS. WHEN I WORKED IN THE BIOTECH INDUSTRY AND THE PHARMA INDUSTRY, WE ACTUALLY INVOLVED SOMETIMES SEVERAL THOUSAND PATIENTS IN THE TRIALS, ANYWHERE FROM A COUPLE OF HUNDRED TO A COUPLE OF THOUSAND. THIS IS TYPICAL FOR NEW AREAS OF RESEARCH ESPECIALLY IN THE AREA OF SAFETY AND EARLY ASSESSMENT OF EFFICACY.

WHEN IT COMES TO PHASE 2 CLINICAL TRIALS, AGAIN, FOUR OF THE CLINICAL TRIALS IN OUR PORTFOLIO ARE IN PHASE 2. TWO IN OPHTHALMOLOGY. THE CLIN2 GRANTS TO TEND TO BE A FOUR-YEAR TERM. BUT THE FOUR GRANTS ON THE SLIDE ARE EITHER EARLY FIRST YEAR OR SOME ARE CLOSER TO THE FOURTH YEAR OR LONGER. SO SEVERAL OF OUR GRANTS PROGRESSED FROM DISCOVERY TO TRANSLATION TO CLIN1 AND CLIN2.

AND SUCH AN EXAMPLE IS THOSE TWO OPHTHALMOLOGY GRANTS THAT ARE SHOWN ON THE SLIDE. THEY WERE AWARDED TO DR. HENRY KLASSEN AND JCYTE CORPORATION, WHICH WAS STARTED BY DR. KLASSEN AND OTHERS. AS YOU CAN SEE HERE, THE TWO GRANTS FUNDED AT DIFFERENT TIMES FOR THE SAME GRANTEE TO ADVANCE THE PROGRAM FURTHER INTO DEVELOPMENT. SO THAT'S

NOT -- IT HAS HAPPENED FREQUENTLY WITHIN THE CIRM, AND THAT'S WHAT WE CALL PROGRESSION EVENTS. AND THAT ALLOWS THE GRANT ACTUALLY TO DO WELL BY THE PATIENTS AS WELL AS BY THE ROBUST SCIENCE THAT THE GRANTEE HAD DEVELOPED.

FINALLY, WE HAVE CIRM ACTIVE TRIALS IN PHASE 3. AND BY THE WAY, THE AREA OF CELL AND GENE THERAPY, THE PROGRESSION OF GRANTS OR PROGRESSION OF CLINICAL TRIALS FROM PHASE 1, 2, AND 3 IS NOT NECESSARILY HOLDING FAST TO NEEDING TO GO ALL THE WAY TO PHASE 3 TO GET APPROVAL. IN OUR PORTFOLIO WE HAVE THREE THAT ARE DIFFERENT, AGAIN, STAGE OF MANAGING THEIR GRANTS. WE HAVE ONE IN NEUROBIOLOGY, ONE IN TRANSPLANTATION, AND ONE IN ONCOLOGY WITH A VASCULAR NICHE THEME TO IT. THOSE GRANTS HAVE -- LIKE THE OTHER SLIDE, THE ONE BY ANGIOCRINE IS NEW. IT JUST GOT APPROVED BY THE BOARD IN THE LAST MONTH.

SO WE HAVE ALL THESE CLINICAL GRANTS. HOW DOES THE CIRM TEAM MANAGE THEM? SO ADVANCING THE PORTFOLIO IS REALLY A DYNAMIC PROCESS THAT ENGAGES THE GRANTEES, CIRM, AND WHEN I SAY CIRM, IT'S THERAPEUTICS DEVELOPMENT, BUT MANY OTHER ALSO LIKE BUSINESS DEVELOPMENT, OFFICE OF THE PRESIDENT, AND OTHERS PARTICIPATE AS NEEDED DURING THE CONDUCT OF THESE CLINICAL ADVISORY PANELS.

PATIENT REPRESENTATIVES ARE A KEY COMPONENT AS WELL AS EXTERNAL EXPERTS. AND WE WORK CLOSELY WITH THE GRANTEE TO IDENTIFY THE EXPERTS AS WELL AS WE COME UP WITH OUR OWN AND MAKE RECOMMENDATIONS. SO THE CLINICAL ADVISORY PANELS HAVE BEEN A SUCCESS FOR US, AND WE HAVE REPLICATED THAT IN THE TRANSLATION AREA AND WE CALL THEM TAP'S, TRANSLATION ADVISORY PANELS. THE PURPOSE OF CAP IS TO PROVIDE GUIDANCE AND ADVICE TO THE PROJECT TEAM. A CAP IS ASSEMBLED BY CIRM FOR EACH CLINICAL STAGE AWARD, AND MULTIPLE CAP MEETINGS OCCUR OVER THE LIFETIME OF THE PROGRAM AWARD.

THE QUESTION YOU MIGHT BE ASKING: DO THESE CAP'S MAKE ANY DIFFERENCE? BEFORE I ANSWER THAT QUESTION, I JUST WOULD LIKE YOU TO ADMIRE WITH ME HOW MANY CAP MEETINGS THAT WE'VE DONE SINCE 2016. WE HAD 356 CAP MEETINGS. BY THE WAY, IT'S QUITE A FEAT TO ACTUALLY ASSEMBLE THOSE GIVEN HOW BUSY EVERYONE IS. WE HAVE INCLUDED 91 EXTERNAL ADVISORS, AND WE INCLUDED 68 PATIENT REPRESENTATIVES. AND THOSE NUMBERS ARE REALLY GROWING AS WE SPEAK.

SO YES, TO GO BACK TO MY EARLIER QUESTION, DO THESE CAPS MAKE A DIFFERENCE, THE ANSWER IS ABSOLUTELY YES AS MEASURED BY WHETHER THE CHALLENGES THAT THE GRANTEES HAVE FACED WERE RESOLVED OR NOT,

THESE GRANTEES RECEIVED THE GUIDANCE THEY NEEDED.

SO I JUST WANTED TO MENTION WHAT ARE SOME OF THE OUTCOMES. FOR SOME OF THE GRANTS MANUFACTURING CHALLENGES WERE OVERCOME. FOR SOME THE CLINICAL TRIAL DESIGN WAS OPTIMIZED THROUGH AMENDMENT. AGAIN, AMENDMENTS GO ALSO TO THE FDA. THEY COME TO US AFTER THE FDA APPROVES THEM. ENROLLMENT IS ENHANCED, AND THIS IS IN CLOSE WORK WITH LIKE THE ALPHA CLINICS OR ANY OTHER CLINICS THAT WE ARE IN THE KNOW WITH AND HELPS THE GRANTEE TO IDENTIFY POTENTIAL NEW INTERESTED PARTIES. REGULATORY ADVICE PROVIDED. WE HAVE EXPERTISE WITHIN CIRM, BUT WE ALSO INVITE EXPERTS FROM THE OUTSIDE, ESPECIALLY THOSE WHO HAVE PARTICIPATED IN GETTING EITHER CELL AND GENE THERAPY APPROVED TO THE MARKET.

WE ARE ACTUALLY STARTING A NEW KIND OF CAP, WHICH IS MARKET APPROVAL ADVISORY PANEL, AND THAT WILL INCLUDE ADVISORS WHO ACTUALLY HAVE HAD A TRACK RECORD OF GETTING CELL AND GENE THERAPY TO MARKET.

THE PARTNERING IS FACILITATED, AND I SAID 50 PERCENT OF OUR GRANTS HAVE BEEN ACTUALLY PARTNERED. AND DEVELOPMENT PATHS DELINEATED. SO THE CAP ADVICE, BASED ON OUR SURVEY THAT WE'VE DONE,

75 PERCENT AND MORE OF OUR CLINICAL AWARDS. I THINK WE ARE ALL HAPPY WITH THAT AND AIMING TO EVEN ADVANCE IT MORE.

SO IN CONCLUSION, THE TRANSLATION AND CLINICAL PORTFOLIO IS DIVERSE AND COVERS MULTIPLE THERAPEUTIC AREAS. SEVERAL OF THE CLINICAL GRANTS ARE IN EARLY DEVELOPMENT CONSISTENT WITH CIRM DERISKING DEVELOPMENT. SOME OF THE GRANTS PROGRESSED TO LATER STAGE DEVELOPMENT, WORKING CLOSELY WITH CIRM WITH REPEAT GRANTS OVER THE YEARS FOR THE SAME PROJECT. AND THEN THE CLINICAL AND TRANSLATIONAL ADVISORY PANELS RESOLVED SEVERAL TECHNICAL, REGULATORY, AND STRATEGIC CHALLENGES AND FACILITATED PARTNERSHIPS.

WITH THAT, I WILL STOP AND THANK YOU. AND HAPPY TO ANSWER ANY QUESTIONS THAT YOU MAY HAVE. DR. GOLDSTEIN, PLEASE GO AHEAD AND ASK.

DR. GOLDSTEIN: THANK YOU, ABLA. TERRIFIC PRESENTATION. I'M JUST INCREDIBLY IMPRESSED AT HOW MANY TRIALS THERE ARE AND LOOK FORWARD TO MORE.

MY QUESTION IS HOW MUCH STANDARDIZATION OF INFORMED CONSENT IS DONE ACROSS THE ALPHA CLINIC NETWORK AND CIRM CLINICAL GRANTS IN GENERAL? I KNOW THEY'RE VERY DIVERSE TECHNOLOGIES, BUT STILL IN PRINCIPLE YOU COULD STANDARDIZE THE BASIC FORM

TALKING ABOUT RISKS AND BENEFITS.

DR. CREASEY: ACTUALLY WE HAVE BEEN WORKING TOWARDS ACHIEVING THE GOAL YOU ARE DESCRIBING. AND SO MAYBE GEOFF CAN ANSWER ABOUT THE ALPHA CLINICS AND STANDARDIZATION OF THE INFORMED CONSENT THERE BECAUSE HE AND I HAVE BEEN DISCUSSING THIS AND HE IS ONTO IT. WE ACTUALLY ARE ASPIRING TO HAVE AS CLOSE OF A STANDARDIZATION OF INFORMED CONSENT ACROSS THE ALPHA CLINICS, BUT ALSO AFFECTING THE GRANTS THAT ARE SUBMITTED TO CIRM. GEOFF, YOU WANT TO SAY ANYTHING ABOUT THAT?

DR. LOMAX: THANK YOU FOR THAT. THANK YOU, DR. GOLDSTEIN. I THINK, AS YOU ALLUDED TO, EACH OF THE AWARDS ARE UNIQUE IN THEIR OWN RIGHT. SO THOSE CONSENTS ARE GOING TO REFLECT THE UNIQUE NATURE OF THE ACTUAL CLINICAL PROTOCOL. AND THAT'S SOMETHING THAT'S NOT SOMETHING THAT, I THINK, WE COULD NECESSARILY STANDARDIZE.

BUT WHAT REALLY, I THINK, HAS COME UP, AND THIS HAS COME UP RIGHT NOW IN THE DISCUSSIONS WITH THE ALPHA CLINICS, WHICH FOR THE REST OF THE GROUP I HAVE A BRIEF PRESENTATION MOMENTARILY THAT I'LL ELABORATE A BIT MORE, BUT I THINK THERE'S A SERIES OF CONSIDERATIONS IN THESE TRIALS IN GENERAL, PARTICULARLY ABOUT DISCLOSURE AND PATIENT EDUCATION,

THAT THE NETWORK IS VERY INTERESTED IN DEVELOPING TOOLS. AND THAT'S REALLY ONE OF THE QUESTIONS WE'RE GOING TO BE ASKING OF THE WORKING GROUP IN THE ENSUING DISCUSSION. WHAT SUPPORT STRUCTURES AND TOOLS CAN THE NETWORK PROVIDE TO REALLY ENABLE ROBUST CONSENT?

THERE HAVE BEEN A NUMBER OF TOPICS THAT HAVE COME UP. I THINK YOU WERE PART OF A DISCUSSION WHERE WE ITEMIZED SOME INITIATIVES THAT ARE GOING ON AND POTENTIAL OUTCOMES. AND PART OF WHAT WE WANTED TO DERIVE FROM TODAY'S DISCUSSION WAS TO REALLY REEVALUATE THAT LIST AND THEN PROVIDE A REPORT BACK TO OUR ALPHA CLINICS NETWORK ON POTENTIAL TOOLS OR RESOURCES THAT COULD BE DEVELOPED IN A NETWORK ENVIRONMENT. SO TO THE POINT OF -- STANDARDIZATION MIGHT BE A STRONG TERM, BUT A STANDARDIZED SET OF TOOLS THAT THE NETWORK COULD UTILIZE, PARTICULARLY BECAUSE THEY ALSO HAVE AN IRB AGREEMENT THAT IS A RELIANCE AGREEMENT ACROSS THE NETWORK.

SO, FOR EXAMPLE, IF THERE WAS STANDARDIZED EDUCATIONAL MATERIAL DISCUSSING A PARTICULAR RISK IN THE GENE THERAPY TRIAL THAT ALL THE IRB'S RECOGNIZED, THEN THAT TOOL COULD BE AVAILABLE, FOR EXAMPLE, TO AN INFORMED CONSENT -- WITHIN THE INFORMED CONSENT PROCESS. AND EVERYONE WITHIN THE

NETWORK WOULD BE ABLE TO UTILIZE THAT IN A CONSISTENT WAY.

SO THOSE ARE SOME OF THE IDEAS THAT HAVE COME UP. AND I THINK, AS YOU WILL HEAR FROM THE NEXT SET OF PRESENTATIONS, WE ARE IN A POSITION TO POTENTIALLY IMPLEMENT SOME OF THOSE OPPORTUNITIES, BUT WE'RE ALSO LOOKING TO MAKE SURE WE ARE GETTING GUIDANCE FROM THIS GROUP AND OTHERS.

DR. CREASEY: DR. GOLDSTEIN, I THINK YOUR POINT IS VERY IMPORTANT IN TERMS OF INFORMED CONSENT, ALSO THE DIVERSITY OF OUR GRANTS. IT'S BEEN ON MY LIST OF THINGS TO ACTUALLY START ACCENTUATING AND THINKING ABOUT EACH OF THE GRANTS SPECIFICALLY, HAVING US EVALUATE AND HELP THEM AND THINK THROUGH THEIR INFORMED CONSENT BEFORE THEY SUBMIT. BUT IT'S AN AREA THAT WE NEED TO VET A LITTLE BIT MORE CAREFULLY AND WORK CLOSELY WITH GEOFF AND SEAN AND THE ALPHA CLINICS. AND SO IT'S ON OUR RADAR. SO STAY TUNED. WE'LL COME BACK TO THAT MAYBE IN ANOTHER SIX MONTHS OR SO AFTER WE'VE THOUGHT SOME MORE ABOUT IT.

DR. GOLDSTEIN: THANK YOU. ONE ISSUE I AM CONCERNED ABOUT IS MAKING SURE THAT ALL OF THE INFORMED CONSENTS SOMEHOW RECOGNIZE THAT EVEN BEYOND THE LIFETIME OF CIRM, THERE MAY BE RISKS OR LOSS OF

EFFICACY OR A VARIETY OF THINGS THAT COULD BE HARD FOR PEOPLE OF VARYING EDUCATION LEVELS TO COMPREHEND OR TO HAVE PRIOR KNOWLEDGE ABOUT.

DR. CREASEY: YES. YES. WE UNDERSTAND. AND SO THAT'S WHY ESSENTIALLY WE ARE BUILDING THE BASICS FOR THE TECHNOLOGIES WE KNOW ABOUT, AND ESPECIALLY WHEN IT COMES TO INFORMED CONSENT FOR NEW TECHNOLOGIES WHERE THE PATIENTS NEED A LITTLE BIT MORE AWARENESS AND NOT ALSO HAVE AN INFORMED CONSENT. WE HAVE BEEN TOLD THAT SOME OF THE INFORMED CONSENTS CAN BE VERY LENGTHY, AND THE PATIENTS NEED, LIKE, A TRANSLATOR IN ORDER TO HELP THEM FIGURE OUT WHETHER THEY WANT TO BE ENROLLED OR NOT. SO WE ACTUALLY -- WE HAVE NOW A GOOD TEAM THAT WE CAN GET ON IT AND BE ABLE TO ADDRESS IT MORE CAREFULLY. AND LIKE I SAID, WE'LL REPORT BACK.

DR. GOLDSTEIN: THANK YOU.

DR. CREASEY: YOU'RE WELCOME. OKAY. DR. WAGNER. I DIDN'T SEE WHO WAS FIRST OR DR. KAHN.

CO-CHAIRMAN KAHN: JOHN IS FIRST.

DR. WAGNER: THAT MAY BE TRUE. BUT, JEFF, IF YOU'RE GOING TO RESPOND ABOUT OR HAVE A STATEMENT RELATED TO THE CONSENTS, THAT MAY BE BETTER NOW. I HAVE SOMETHING TOTALLY DIFFERENT.

CO-CHAIRMAN KAHN: OKAY. SURE. I JUST

WANT TO ASK A QUESTION, ABLA. VERY INTERESTING AND INFORMATIVE. AND FOLLOWING ON DR. GOLDSTEIN'S QUESTION, IS THERE ANY INTERACTION WITH IRB'S AT EACH OF THE INSTITUTIONS WHERE THESE PROJECTS ARE BEING UNDERTAKEN AS A WAY OF KIND OF NETWORKING FOR THE PURPOSE OF SOME KIND OF STANDARDIZATION ON SOME OF THE CONSENT ISSUES? MAYBE GEOFF WILL TALK ABOUT THAT IN THE ALPHA NETWORKS PRESENTATION.

DR. CREASEY: THE ABILITY TO DO THAT IS THERE FOR THE ALPHA CLINICS. BUT WHEN PEOPLE APPLY TO CIRM, AND OUR REQUIREMENT TO RUN A CLINICAL TRIAL IS THAT THEY HAVE AN IND AND THEIR CLINICAL PROTOCOL HAS BEEN APPROVED BY THE FDA, THAT ALSO SUGGESTS THEIR IRB ALREADY IS ON TRACK. SO IT'S HARDER TO PUT, LIKE, IMPLEMENT OR KIND OF MODIFY ANYTHING RELATED TO THE IRB.

BUT PART OF OUR -- WE ACTUALLY CALL OUR CAMPAIGN FOR ATTRACTING PEOPLE TO APPLY TO CIRM HUNTING. AND SO WHEN WE HUNT FOR POTENTIAL GRANTS, THAT'S AN OPPORTUNITY TO RAISE THE ISSUES SUCH AS HAVE YOU TALKED TO YOUR IRB ABOUT INFORMED CONSENT? AND IS IT IN THE RIGHT SHAPE FOR THIS NEXT GENERATION OF GENE THERAPY OR SRNA THERAPY OR WHATEVER? THAT WILL BE MAINLY AN AWARENESS CAMPAIGN RATHER THAN US INFLUENCING IN THE NEAR TERM.

CO-CHAIRMAN KAHN: YEAH.

DR. LOMAX: JUST TO ADD TO THAT RESPONSE, KEEP IN MIND THERE IS A REAL GRADATION OF HOW THESE AWARDS COME THROUGH THE CIRM SYSTEM. SOME ARE ENTIRELY INDEPENDENT. THEY'VE REALLY COME IN EXTERNALLY AND THEY'VE BEEN DEVELOPED OUTSIDE OF SORT OF THE CIRM DEVELOPMENT PIPELINE, BUT UTILIZE -- THEY'RE TREATING PATIENTS IN CALIFORNIA, WHICH OUR CLINICAL TRIAL OPPORTUNITIES HELP ENABLE.

AND THAT EXAMPLE IN CONTRAST TO WE HAVE A NUMBER OF PROJECTS THAT ACTUALLY ARE BEING DEVELOPED IN MULTIPLE ALPHA CLINICS CURRENTLY. AND PROGRAMS LIKE THAT, THERE IS VERY ROBUST DISCUSSION BETWEEN THE CLINICS. AND SO IN THOSE TYPES OF EXAMPLES, THERE'S MORE OF A DEVELOPMENT OF THESE PROTOCOLS WITH THE BACKGROUND OF HAVING AN IRB RELIANCE AGREEMENT. SO IT JUST -- IT'S HARD TO SORT OF GENERALIZE. IT REALLY DEPENDS SORT OF HOW THE TRIAL'S COMING THROUGH THE PIPELINE, HOW IT'S BEING DEVELOPED. SO IT WILL VARY IS JUST REALLY MY POINT THERE.

BUT SOME OF THE DISCUSSIONS BETWEEN THE DIFFERENT SITES AND THE IRB'S I'VE FOUND INCREDIBLY ROBUST, IF YOU WILL. USE OF INTERACTIVE TOOLS, IPADS WHERE PATIENTS -- IT'S NO LONGER A PIECE OF

PAPER. IT'S DYNAMIC TOOLS, TRYING TO DEVELOP THOSE TOOLS IN A WAY THAT YOU'RE LEARNING FROM THE QUESTIONS THEY'RE ASKING AND CONTINUALLY REEVALUATING. SO THERE ARE A NUMBER OF EFFORTS WITHIN OUR NETWORKS TO REALLY TRY TO DO FIRST-RATE EDUCATION, CONSENT, AND USING THESE SORT OF DYNAMIC RESOURCES.

CO-CHAIRMAN KAHN: SOME OPPORTUNITY FOR BEST PRACTICES. WE CAN CONTINUE TO TALK ABOUT THIS, OF COURSE. THANKS.

DR. WAGNER: ABLA, I REALLY SEE ALL THE SUCCESSES THAT HAVE BEEN MADE. I THINK THAT PART OF THE MISSION OF THIS GROUP IS WHERE DO WE SEE OPPORTUNITIES, AS WE JUST DISCUSSED, AND HOW WE CAN DO THINGS BETTER. ONE THING AS I WAS THINKING ABOUT -- WELL, THERE'S TWO THINGS IN PARTICULAR AS I WAS THINKING ABOUT THIS AS YOU WERE SPEAKING.

BECAUSE YOU MENTIONED THE TERM "DERISKING" IN THE EARLY STAGES OF DEVELOPMENT, BUT ALSO TALKING ABOUT THE CLINICAL ADVISORY PANELS AND HOW THEY WERE ABLE TO ACHIEVE CERTAIN OUTCOMES THAT WOULD FURTHER DERISK, WHAT I THINK IS IMPLIED, BUT NOT REALLY FORMALLY MENTIONED IS THAT DERISKING WOULD BE, IN MY MIND, IS HOW DO WE AS A GROUP INCREASE THE PROPORTION OF STUDIES THAT BEGIN IN EARLY

DEVELOPMENT, PHASE 1, AND SUCCEED THROUGH THE TRANSLATIONAL PIPELINE?

AS YOU KNOW, THE MAJORITY OF TRIALS FAIL MOST IN PHASE 2 AND MANY IN PHASE 1. AND SO HOW DO WE FURTHER DERISK THAT AND THE SUCCESS IN GETTING IT TO THE NEXT PHASE? AND SO I THINK THAT, AS YOU THINK ABOUT THE METRICS OF THE SUCCESS OF THIS WORK, SOMEHOW THAT MIGHT BE TAKEN INTO ACCOUNT OF HOW DO WE ASSURE THAT THE INFORMATION PROVIDED, WHETHER -- WHAT I HEARD, AND THIS IS TO SIMPLIFY MORE THAN WHAT YOU SAID, WAS THAT YOU'RE DERISKING IN SOME WAYS BY PROVIDING A PERHAPS POTENTIALLY BETTER PATHWAY IN THE PHASE 1 CLINICAL TRIAL DESIGN. I'M ADDING WORDS TO WHAT YOU SAID.

IN ADDITION, ALSO, IT COULD BE DERISKING A PATHWAY TO GETTING FDA APPROVAL FOR THE FIRST IND. ALL THOSE THINGS ARE STILL VERY IMPORTANT PARTS OF THE PROCESS, BUT THEN ULTIMATELY WHAT THE AIM OF CIRM IS IS TO HAVE A SUCCESSFUL THERAPY THAT IS THROUGH THE PIPELINE, THAT HAS A DEMONSTRABLE IMPACT ON THE SURVIVAL, LIFE OF INDIVIDUALS. SO IT'S PART OF A COMMENT, BUT ALSO LIKE FRYING TO FURTHER DISCUSS WHAT DERISKING MEANS. AND THAT'S, AGAIN, PART OF THIS ORGANIZATION MOVING FORWARD IS HOW CAN WE DO EVEN MORE THAN WHAT'S CURRENTLY BEING DONE?

IT'S A COMMENT, A STATEMENT ABOUT THE TERM "DERISK."

THE SECOND THING IS THAT, AS I THINK ABOUT WHAT WAS SAID IN THE VERY BEGINNING OF THE CONVERSATION ABOUT PART OF THIS STANDARDS WORKING GROUP IS TO THINK ABOUT HAVING A PRODUCT AT THE END OF THE DAY THAT HAS GREAT IMPACT FOR ALL PEOPLE WITHIN THE STATE, FOR ALL PEOPLE IN THE WORLD. WHEN YOU GO BACK AND THINK ABOUT THE SUCCESS OF SOME RECENT STUDIES, LET'S SAY, CAR-T CELLS FOR CD 19 POSITIVE LYMPHOMA LEUKEMIA. WHAT WE DON'T KNOW IS THAT MOST OF THE WORLD CAN'T GET ACCESS TO THIS EVEN THOUGH IT'S SO PROMISING AND REPRESENTS THIS NEW GREAT FIELD OF INTEREST, BUT BECAUSE OF COST, BECAUSE OF LOGISTICS IS NOT REALLY ACCESSIBLE TO THE MAJORITY OF THE WORLD. RIGHT NOW IT'S NOT EVEN ACCESSIBLE EASILY TO PEOPLE WITH NEWLY DIAGNOSED DISEASE BECAUSE, UNTIL WE HAVE AN OFF-THE-SHELF PRODUCT THAT'S READILY AVAILABLE DAY ZERO, UNLESS THE DIAGNOSIS IS MADE, IT LIMITS US.

MORE IMPORTANTLY, I THINK IT'S JUST TO ACKNOWLEDGE THE FACT THAT, EVEN THOUGH WE HAVE THIS GREAT THERAPEUTIC, AND YET IT'S NOT AVAILABLE TO MANY PEOPLE, THINK ABOUT ALSO THE RECENT EXPERIENCE WITH ADRENLEUKODYSTROPHY AND GENE THERAPY WITH COUNTRIES IN EUROPE SAYING WE ARE NOT EVEN GOING TO

OFFER IT BECAUSE IT'S TOO EXPENSIVE.

SO THE ONE THING YOU ALSO POINTED OUT, WHICH IS IMPORTANT AND I THINK IS GOOD ON THE ONE HAND, IS THAT A SIGNIFICANT PROPORTION OF THE STUDIES OR TRIALS ARE COSPONSORED BY INDUSTRY. AND YET ONE OF CIRM'S MISSIONS MOVING FORWARD IS MAKING THIS AVAILABLE AND LOOKING AT COSTS. AND YET WHEN YOU HAVE A PRODUCT THAT'S COMING THROUGH INDUSTRY, THERE'S ONLY, I THINK, SO MUCH CIRM CAN DO. OR I SHOULD NOT PUT IT THAT WAY. IT SHOULD BE THAT WE SHOULD BE THINKING ABOUT WHAT CIRM MIGHT BE ABLE TO DO TO MAKE SURE THAT THE INTENTIONS ARE ALL ACHIEVABLE; THAT ONCE IT MOVES TO INDUSTRY, IS THERE ANY GUIDANCE OR GUIDELINES OR WHATEVER THAT CIRM CAN PLAY A ROLE IN TO ENSURING THAT WHAT YOU BELIEVE YOUR MISSION IS IS SOMETHING THAT AT THE END OF THE DAY IS REALLY ACHIEVABLE OR NOT.

DR. CREASEY: THANK YOU VERY MUCH. YOU SAID A LOT, AND YOU SAID A LOT OF VERY IMPORTANT THINGS THAT ARE ACTUALLY ON OUR MIND. AND WE HAVE -- WE ARE THINKING ABOUT HOW TO FACILITATE GETTING, LIKE, THE THERAPIES SUCH AS CAR-T AVAILABLE TO OTHER DIVERSE GROUPS WITHIN THE U.S. AND OUTSIDE, ET CETERA. THERE ARE ALL KINDS OF PROGRAMS THAT HAVE COME BEFORE US, AND WE ARE ENTERTAINING HOW TO

WORK CLOSELY WITH SUCH PROGRAMS. BUT OUR MAIN TASK TODAY WAS TO JUST FAMILIARIZE YOU WITH WHAT OUR ACTIVE CLINICAL TRIAL GRANTS LOOK LIKE. BUT STAY TUNED. I'M GLAD YOU ARE A MEMBER OF THE STANDARDS COMMITTEE. SO WE ARE EMBARKING ON OTHER ACTIVITIES AND WE'LL BRING THEM BEFORE YOU WHEN WE ARE READY. MAYBE DR. MILLAN WOULD LIKE TO ADD.

DR. MILLAN: I JUST WANT TO RESPECT THE CHAIR OF THE SWG IF YOU WANTED TO CONTINUE THIS CONVERSATION. BUT IN RESPONSE, I THINK THIS IS THE PURPOSE OF HAVING THESE CONVERSATIONS AT THE STANDARDS WORKING GROUP IS THAT THERE ARE A LOT OF -- WITH THE SUCCESS OF MORE OF THESE PROGRAMS MAKING THEIR WAY THROUGH LATER STAGE RESEARCH THAT WE ARE FACED WITH THESE CHALLENGES. SO WE REALLY DO APPRECIATE THE CONVERSATIONS WITH THIS GROUP. IT IS ALL IN DEVELOPMENT, AND WE REALLY DO VALUE THE INPUT AND THE DIRECTION THAT THIS GROUP CAN PROVIDE US AS WE EVALUATE HOW WE CAN IMPACT. BEING A FUNDING AGENCY, WE CAN IMPACT BY THE TERMS OF AWARDS, THE REVIEW CRITERIA FOR THE AWARDS.

SO THERE ARE ALL SORTS OF WAYS THAT WE CAN INFLUENCE. SO YOUR GUIDANCE WILL BE VERY IMPORTANT TO US BECAUSE THERE ARE VARIOUS WAYS ALONG THE LINE OF BOTH GRANTING AND PARTNERING AND MANAGING THESE

PROGRAMS, BOTH WITH OUR INDUSTRY GRANTEES AND OUR ACADEMIC GRANTEES, THAT WE HOPE TO BE ABLE TO BRING IT FORWARD WITH THE OBJECTIVE OF EQUITABLE ACCESS AND TRULY BRINGING IT OUT TO THE COMMUNITY, NOT JUST HAVING AN INITIAL SUCCESS, BUT TRULY HAVING SUCCESS OF IMPACTING THE HEALTHCARE LANDSCAPE.

A VERY GENERAL RESPONSE, BUT I JUST WANTED TO RESPOND TO ABLA'S REQUEST FOR ME TO SAY SOMETHING. THANK YOU.

DR. CREASEY: THANK YOU, MARIA. SWG CHAIRS, WOULD YOU LIKE ME TO CONTINUE OR STOP?

CO-CHAIRMAN KAHN: I THINK WE ARE OKAY. WE CAN KEEP GOING. FRED HAS GOT HIS HAND UP.

CO-CHAIRMAN FISHER: THIS CONVERSATION, WHICH IS GREAT, A WHILE AGO THE IDEA OF UNDERSTANDING WHAT THE ROLE OF IRB IS IN THIS, AND THEN JEFF KAHN ELABORATED ON THAT. AND IT HAS ME WONDERING IF OUR EFFORTS KIND OF HAVE A BLIND SPOT AROUND IRB AND WHETHER WE SHOULD BE INCLUDING IN THE COMPOSITION OF THIS GROUP SOMEONE WITH DEEP IRB EXPERIENCE SO THAT WE DON'T FIND OURSELVES DEVELOPING THINGS THAT MAYBE THE CLINIC WILL GO FOR AND MAYBE THE RESEARCHERS WILL GO FOR AND THE COMPANIES WILL GO FOR, BUT THERE MIGHT BE A LAND MINE WAITING FOR US WITH IRB AND HOW DO WE INTEGRATE

THAT INTO OUR WORK SO THAT WE ARE TAKING A TRULY INCLUSIVE APPROACH. MAYBE WE ALREADY ARE, BUT THOSE WERE THE THOUGHTS THAT I HAD CONNECTED TO THIS DISCUSSION.

DR. LOMAX: JUST ONE THING TO ADD THERE. UNFORTUNATELY MELISSA LOPES COULDN'T JOIN US FOR THIS PARTICULAR MEETING DUE TO TRAVEL, BUT SHE DOES SIT IN THE EMBRYONIC STEM CELL OVERSIGHT COMMITTEE IRB SPACE. AND WE ALSO ALWAYS HAVE THE OPPORTUNITY TO BRING IN OUTSIDE EXPERTS TO ADVISE AS WELL. SO IT'S CLEARLY A CRITICAL NEED. AND TO THE EXTENT WE'VE TRIED TO ADDRESS IT, I DON'T KNOW IF THAT'S SUFFICIENT, BUT THERE IS REPRESENTATION THERE IN TERMS OF THE STANDING COMMITTEE.

CO-CHAIRMAN FISHER: I THINK THAT'S GREAT TO KNOW. AS THIS GROUP SORT OF GETS UNDER WAY AGAIN, IT'S GREAT TO KNOW AND FOR EVERYONE TO KEEP IN MIND THAT WE CAN BRING IN OUTSIDE EXPERTISE IF WE FEEL LIKE THERE'S A TOPIC THAT'S BEING CONSIDERED THAT THE GROUP WANTS ANOTHER KEY INFORMANT TO PARTICIPATE, THAT WE CAN DO THAT. THAT'S GREAT.

CO-CHAIRMAN KAHN: FRED, BETWEEN MELISSA AND I, I THINK WE HAVE A LOT OF KNOWLEDGE AND EXPERTISE ABOUT HUMAN SUBJECT RESEARCH POLICY. BUT YOUR POINT ABOUT, I THINK, IRB COLLABORATION AND

INSIGHTS ON THE IMPLEMENTATION WOULD BE REALLY HELPFUL AS WE GET DEEPER INTO THAT. SO I THINK THAT'S A REALLY HELPFUL POINT FOR US TO KEEP IN MIND AS WE GO FORWARD. IT'S SORT OF EASY TO TALK ABOUT POLICIES AND APPROACHES, BUT IT'S THE DOING THAT'S REALLY IMPORTANT IN THIS INCREASINGLY COMPLICATED AND, ABLA, YOUR POINT ABOUT VERY LONG CONSENT FORMS THAT ARE FULL OF DETAIL AND OFTEN REALLY COMPLICATED TERMINOLOGY AND CONCEPTS, IT'S NOT NEW. BUT I THINK IT'S MAYBE EVEN MORE THE CASE AS THESE TECHNOLOGIES EVOLVE IN THESE CLINICAL TRIALS WITH INCREASINGLY COMPLEX TECHNOLOGIES GOING FORWARD. REALLY IMPORTANT TO KEEP THAT ON OUR LIST.

DR. CREASEY: I AGREE. I AGREE. THANK YOU.

DR. LOMAX: MAYBE IF I MAY JUST ADD ONE OTHER POINT. I WAS ACTUALLY GOING TO RAISE IT. IT COMES UP IN A LATER SLIDE, BUT IT'S ON TOPIC NOW, SO I'LL MENTION IT. IF YOU REMEMBER, I ALLUDED TO THE EVALUATION OF OUR ORIGINAL POLICIES THAT WE DID WITH OUR GRANTEE INSTITUTIONS. THAT WAS SORT OF PHASE 2 OF THE SLIDES I PRESENTED EARLIER. AND NOW WITH OUR ALPHA CLINICS NETWORK, WHICH I'LL DESCRIBE AGAIN MOMENTARILY, WE DO HAVE THE OPPORTUNITY TO REALLY SIT DOWN AT THAT LEVEL, WHETHER IT BE THE IRB, THE

STEM CELL RESEARCH OVERSIGHT COMMITTEES, THE REGULATORY LAYER OF THESE INSTITUTIONS, WE HAVE MODELS THAT WE'VE IMPLEMENTED MANY TIMES WHERE WE ARE ABLE TO REALLY SIT DOWN AND HAVE VERY IN-DEPTH CONVERSATIONS ABOUT THESE SORT OF OPERATIONAL ISSUES.

SO TO THE EXTENT WE THINK THERE ARE RESEARCH NEEDS OR CONVERSATIONS THAT WOULD BE HELPFUL, I, AGAIN, THINK WE'RE IN A POSITION TO FACILITATE THOSE DISCUSSIONS AND BRING THAT BACK TO THE WORKING GROUP IN SOME MANNER. SO JUST TO -- AGAIN, THAT WILL BE A POINT.

IT'S ONE OF THE QUESTIONS WE ACTUALLY HAD FOR YOU LATER ON WAS ARE THERE AREAS WHERE WE MIGHT -- IS THERE SOME ETHICS POLICY RESEARCH AREAS WE MIGHT WANT TO CONSIDER? SO I'LL JUST PUT THAT ONE OUT EARLY.

CO-CHAIRMAN FISHER: FROM A PATIENT ADVOCATE POINT OF VIEW, I HAVE BEEN CONFRONTED WITH SEVERAL DIFFERENT PATIENT CONSENT EXPERIENCES. AND A COUPLE OF PEOPLE ON THIS CALL REFERENCED HAVING JUST FINISHED A SURGERY. THOSE, IN MY EXPERIENCE, PATIENT CONSENT FORMS AROUND SURGERY IS REALLY ABOUT LIMITING THE HOSPITAL'S LIABILITY BECAUSE YOU'RE BASICALLY TELLING THEM THAT YOU UNDERSTAND YOU MIGHT

NOT SURVIVE THE PROCEDURE. AND THAT'S SUPPOSED TO BE OKAY AND SOMEHOW MY SIGNATURE ACKNOWLEDGING THAT MAKES A DIFFERENCE.

FROM A RESEARCH POINT OF VIEW, I'VE ALSO BEEN PART OF RESEARCH IRB'S WHERE THE PERSON GOING -- NOT IRB'S -- INFORMED CONSENT, THE PERSON DOING THE INFORMED CONSENT PROCESS DOES THEIR BEST TO SKIP OVER ALL THAT INTENSE LANGUAGE AND BASICALLY CUT TO THE CHASE. IF YOU'VE EVER BOUGHT A CAR, THEY LIKE RUN THROUGH THE STUFF OR GONE THROUGH A PROCESS WHERE YOU'RE JUST INITIALING. KIND OF LIKE WHEN YOU'VE EVER GOTTEN A MORTGAGE. YOU'RE INITIALING A ZILLION THINGS, AND WHOEVER IS TAKING YOU THROUGH IT IS GIVING YOU THE SHORTHAND VERSION OF STUFF. SO SOMEONE GOES TO A LOT OF TIME CREATING VERY COMPLICATED INFORMED CONSENT PROCEDURES FOR RESEARCH.

AND THEN IT SEEMS, IN MY EXPERIENCE, THAT THE NURSE COORDINATOR'S JOB ENDS UP BEING DISTILLING ALL THAT LANGUAGE DOWN INTO THE SIMPLEST FORM JUST SO YOU CAN MOVE FORWARD AND SIGN IT BECAUSE IN THE END THEY'VE DECIDED AND YOU'VE DECIDED YOU WANT TO BE PART OF THIS THING. THE INFORMED CONSENT PROCESS HAPPENS BASICALLY AFTER EVERYBODY HAS DECIDED, YEAH, LET'S DO THIS. AND SO THERE ARE SHORTCUTS THAT

PROBABLY DON'T COME AS ANY BIG SURPRISE TO ANYBODY HERE.

AND SO I LIKE TO NOT PRETEND THAT I'M IN A WORLD THAT I'M NOT IN. THOSE RESEARCH INFORMED CONSENT FORMS PRETEND LIKE THE PATIENT IS ACTUALLY DIGESTING ALL OF THAT CONTENT IN THOSE FORMS WHEN IN REALITY THEY LIKELY ARE NOT. AND KEEP THAT IN MIND AS WE ARE MOVING FORWARD.

CO-CHAIRMAN KAHN: GEOFF LOMAX, WHERE ARE WE ON TIME?

DR. LOMAX: WE WERE AIMING FOR A BREAK AROUND ELEVEN. SO WE COULD, I THINK, MAYBE IF NOT CUT OFF CONVERSATION, BUT I THINK WE CAN GET THROUGH THE NEXT TWO PRESENTATIONS IN ABOUT 15 MINUTES. SO IF WE CAN GET STARTED IN A FEW MINUTES ON THOSE, I THINK WE'LL STILL BE RIGHT ON TIME AND WE CAN TAKE A BREAK AT ELEVEN.

CO-CHAIRMAN KAHN: JOHN WAGNER, YOU WANT THE LAST WORD ON THIS?

DR. WAGNER: IT WON'T BE THE LAST WORD, I'M SURE. WHAT I CAN SAY IS THAT FOR THOSE OF YOU AT CENTERS WHERE THEY RECENTLY HAVE SUBMITTED RENEWAL FOR YOUR CTSA GRANTS, AS WE DID, THE FOCUS NOW IS ON THE SCIENCE OF TRANSLATIONAL MEDICINE RATHER THAN ON JUST SUPPORTING THE INFRASTRUCTURE

FOR TRANSLATIONAL MEDICINE. AND IT'S REALLY A DIFFERENT TWIST ON ALL OF THIS WHICH REALLY PLAYS IN WELL TO WHAT OUR CONVERSATION IS NOW BECAUSE AT LEAST A NUMBER OF US HAVE HAD CONVERSATIONS ABOUT HOW DO WE IMPROVE THE CONSENT PROCESS USING NEW TECHNOLOGIES, BUT THEN MAKING ITSELF A SCIENTIFIC QUESTION.

SO I COULD SEE -- WITHIN THE CIRM INSTITUTIONS, I CAN SEE OR OUTSIDE CIRM THAT THERE'S AN OPPORTUNITY OF ACTUALLY MAKING IT INTO A SCIENTIFIC QUESTION AND ASKING DOES THIS NEW APPROACH MAKE THE CONSENT PROCESS MORE MEANINGFUL. AND, AGAIN, WITH THESE NEW TECHNOLOGIES THAT ARE AVAILABLE, IT'S REALLY AN INTERESTING TIME TO RELOOK AT THE CONSENT AND SOMETHING TO THINK ABOUT.

DR. LOMAX: THAT IS A PERFECT SEGUE. IF I MAY MOVE TO THE ALPHA CLINICS UPDATE.

CO-CHAIRMAN KAHN: GOOD IDEA.

DR. LOMAX: THANK YOU. IF YOU CAN DO THE NEXT SLIDE. SO WE ARE ACTUALLY IN THE PROCESS CURRENTLY OF ISSUING NINE ALPHA CLINIC AWARDS. THE ALPHA CLINICS ARE A CLINICAL PLATFORM. THEY'RE DESIGNED SPECIFICALLY TO SUPPORT CELL AND GENE THERAPY CLINICAL TRIALS. THEY DON'T FUND THE ACTUAL TRIALS. WHAT THEY FUND IS THE WRAP-AROUND

INFRASTRUCTURE TO ALLOW THOSE TRIALS TO PROCEED SUCCESSFULLY. SO THE STRUCTURE INCLUDES WHETHER IT'S THE MANUFACTURING OR HANDLING OF PRODUCT. SO THERE'S A CELL PHARMACY ASPECT TO A NUMBER OF THESE AWARDS WHERE THEY'RE SUPPORTING GMP FACILITIES OR CELL PROCESSING OR PRODUCT PROCESSING FACILITIES.

MANY OF THE -- ALL THESE AWARDS HAVE A SUBSTANTIAL RESEARCH COORDINATOR COMPONENT. SO THESE ARE RESEARCH COORDINATORS THAT ARE FLUENT AND UNDERSTAND THE TECHNOLOGIES SPECIFICALLY RELATED TO CELL AND GENE THERAPY. THERE ARE CLINICAL EXPERTISE. AND DRAWING OFF OF DR. WAGNER'S POINT, I DON'T WANT TO SAY ALL BECAUSE IT MAY NOT BE A TRUE STATEMENT, BUT OVERWHELMINGLY THE CTSA'S ARE INTEGRAL TO THESE AWARDS. THEY'RE COLLABORATIONS WITHIN THE INSTITUTIONS THROUGH THEIR CTSA'S. SO THERE IS, I THINK, A TRUE OPPORTUNITY TO SORT OF LEVERAGE THE INITIATIVES THAT DR. WAGNER WAS REFERRING TO WITHIN OUR NETWORK.

WHAT IT AMOUNTS TO REALLY IS HORIZONTAL INTEGRATION OF CELL AND GENE THERAPY EXPERTISE ACROSS THE MEDICAL CENTERS SO THAT, WHEN ANYONE COMES TO ONE OF THESE CENTERS, WE CAN RAPIDLY SUPPORT A TRIAL. AND THESE TRIALS COULD EITHER BE CIRM-FUNDED TRIALS OR COMMERCIAL TRIALS WITH

COMMERCIAL SPONSORS THAT HAVE NO CIRM FUNDING, AND THEY COME IN AS A TRADITIONAL SPONSOR. BUT WHAT THEY'VE GOT IS THE ABILITY AT THESE SITES TO RAPIDLY BRING IN A CELL AND GENE THERAPY TRIAL.

IN ADDITION, THE POINT OF A NETWORK IS SORT OF YOU SAY IT'S THE ONE PLUS ONE EQUALS THREE IDEA, THAT WE TRULY -- THE WAY THESE APPLICATIONS WERE SET UP, WE ASKED THE SITES TO REALLY PROPOSE SORT OF VALUE-ADDED OPPORTUNITIES AND NETWORKING OPPORTUNITIES THAT WOULD REALLY DERIVE VALUE. GO TO THE NEXT SLIDE PLEASE.

AND REALLY THESE SORT OF, IF YOU WILL, THESE LANES WHERE THEY'VE PROPOSED PROGRAMMATIC ACTIVITIES THAT WILL RESULT IN VALUE ARE, FIRST OF ALL, IN THEIR CLINICAL PLATFORMS, SO TOOLS FOR DEVELOPING THE THERAPIES, THE CAPACITY TO REALLY COORDINATE RESEARCH. AND SO WE HAVE A FAIR NUMBER OF TRIALS THAT ARE OPEN AT MULTIPLE SITES. AND THERE'S, AGAIN, A LOT OF CROSSTALK AMONG THE SITES WHEN BRINGING THOSE TRIALS IN. THERE'S REGULATORY EXPERTISE AND DEVELOPMENT OF MOU'S. PROBABLY THE MOST SIGNIFICANT IN TERMS OF THIS DISCUSSION BEING A COMMON IRB RELIANCE AGREEMENT. AND THERE'S SORT OF TOOLS THEY DEVELOP THAT ALLOW, AGAIN, FOR MULTIPLE SITE START-UP.

SO ON THE THERAPY SIDE, THERE'S A NUMBER OF COLLABORATIONS, SHARED USE OF GMP FACILITIES, GENOMICS TOOLS, AND GENE EDITING TOOLS AND TECHNOLOGIES. AND IN THIS PARTICULAR ROUND, WE PUT A STRONG EMPHASIS AND REQUIREMENT ON ACCESS AND INCLUSIVITY. SO THERE'S PATIENT REGISTRIES, THE USE OF SHARED REGISTRIES AND PROTOCOLS FOR IDENTIFYING PATIENT POPULATIONS. THERE'S A NUMBER OF EFFORTS PROPOSED TO REALLY EXPAND THE COMMUNITY ENGAGEMENT EFFORTS, WHICH MEANS REALLY GETTING OUT INTO THE COMMUNITY, GETTING AWAY FROM THE ACTUAL MEDICAL CENTER AND INTO THE COMMUNITY, AND FOLLOWING THAT UP WITH ACTIVE PATIENT NAVIGATION.

AND SORT OF UNDERLYING ALL THESE EFFORTS IS BUILDING THE WORKFORCE AND TRAINING AND EDUCATION THAT'S NOW A CENTERPIECE OF ALL THE MAJOR CIRM PROGRAMS. SO THERE'S A SORT OF CROSS-CUTTING EDUCATIONAL COMPONENT TO THIS PROGRAM. AND LIKE I SAY, AS I MENTIONED, WE ARE JUST INITIATING NINE NEW AWARDS. AND I REALLY WANT TO SORT OF FLAG THIS AS AN OPPORTUNITY BECAUSE A NUMBER OF THE AWARDS ALREADY INDICATED AN INTEREST IN SORT OF ETHICAL ISSUES AND WORKING WITHIN CTSA'S AND REALLY CITING SOME OF THE EFFORTS THAT DR. WAGNER ALLUDED TO.

SO TO THE EXTENT, AGAIN, THERE'S THINKING

IN THIS GROUP IN TERMS OF, AGAIN, EITHER RESEARCH NEEDS OR ACTIVITIES THAT WE THINK WOULD BE PARTICULARLY PRODUCTIVE, WE HAVE THE OPPORTUNITY REALLY TO FEED THAT BACK INTO THE NETWORK AS WE DEVELOP PLANS MOVING FORWARD OVER THE NEXT FIVE YEARS. THESE ARE FIVE-YEAR AWARDS.

SO WE ARE STARTING PRETTY MUCH AT DAY ZERO, AND THAT'S ONE OF THE REASONS WE WANTED TO HAVE THIS CONVERSATION WITH YOU ALL THIS MORNING. SO WITH THAT, I THINK I'LL STOP THERE. I THINK IT'S JUST TWO SLIDES, BUT MAYBE WE CAN CHECK. I WAS WRONG LAST LIME. GREAT. SO I DON'T KNOW IF THERE'S ANY QUESTIONS ABOUT THE NETWORK OR ANYTHING THERE.

CO-CHAIRMAN KAHN: I DON'T SEE ANY HANDS. ONE THING, GEOFF, MAYBE NOT FOR THIS MEETING OBVIOUSLY, BUT MAYBE IN THE FUTURE WE COULD HEAR FROM FOLKS WHO ARE FUNDED THROUGH THIS MECHANISM TO SEE WHETHER THEY HAVE SOME ISSUES THAT WE CAN BE HELPFUL WITH. IT'S A LITTLE HARD FOR US TO BE PROACTIVE, I THINK. WE CAN DO IT BOTH WAYS, THINGS THAT WE SEE, BUT ALSO HEARING FROM THE FUNDEES.

DR. LOMAX: WE WOULD BE HAPPY TO FACILITATE THAT. I THINK THAT WOULD BE A GREAT OPPORTUNITY FOR CROSSTALK. WE MAY HAVE SOME REPRESENTATIVES FROM THE NETWORK JOINING. WE DID

TRY TO HAVE A FEW FOLKS. I THINK WE MAYBE RAN THIS MEETING A LITTLE TOO CLOSE TO THE HOLIDAYS AND IT'S A BIT TRICKY FOR SOME. BUT THAT'S ABSOLUTELY SOMETHING I'M SURE THE NETWORK WOULD WELCOME.

CO-CHAIRMAN KAHN: I KNOW WE TRIED TO GET PEOPLE. I SEE SEAN IS UNMUTED. MAYBE HE WANTS TO TALK.

DR. LOMAX: WHY DON'T WE MOVE ON. ACTUALLY, DR. GOLDSTEIN, DO YOU HAVE A COMMENT?

DR. GOLDSTEIN: ONE MORE. WELL, I HAD A QUESTION ABOUT THE ALPHA CLINIC NETWORK, GEOFF. I MEAN YOU'VE DONE A LOVELY JOB DESCRIBING WHAT IS POTENTIALLY A LARGE CAPACITY. SO I GUESS THE QUESTION, WHICH IS PARTLY A STANDARDS QUESTION AND PARTLY AN OPERATIONAL QUESTION, DOES THE ALPHA CLINIC NETWORK HAVE THE CAPACITY TO BRING A THERAPY TO REGISTRATION IN THE ABSENCE OF INDUSTRY INVOLVEMENT?

DR. LOMAX: I WOULD HESITATE TO ANSWER THAT QUESTION BECAUSE I DON'T KNOW WHAT THE ANSWER IS, BUT IT'S CERTAINLY ONE WE CAN ASK.

DR. GOLDSTEIN: IT'S WORTH THINKING ABOUT BECAUSE ONE OF THE ETHICAL ISSUES IN TRIALS, OF COURSE, IS ACCESS TO TRIALS EVEN WHEN THERE'S NOT A COMPANY SUPPORTING THE TRIAL DIRECTLY.

DR. MILLAN: GEOFF, DID YOU WANT ME TO COMMENT ON THAT?

DR. LOMAX: PLEASE.

DR. MILLAN: DR. GOLDSTEIN, THAT'S A REALLY EXCELLENT POINT BECAUSE THIS IS A TOPIC THAT'S ARISEN ON MULTIPLE OCCASIONS BECAUSE ABOUT A THIRD OF OUR PORTFOLIO ACTUALLY IS IN RARE DISEASE WITH CELL AND GENE THERAPY WHERE THIS IS A VERY IMPORTANT TOPIC WHERE SMALL NUMBERS, IT DOESN'T HAVE THE INTEREST OR IT'S NOT REALLY ON THE RADAR OF MOST COMPANIES TO BRING IT FORWARD TO COMMERCIALIZE IT EXCEPT FOR PERHAPS IT'S INTO A PLATFORM APPROACH, FOR INSTANCE. BUT TYPICALLY THAT IS -- A LOT OF THOSE PROGRAMS ARE AT RISK IN TERMS OF, EVEN IF THERE'S STRONG PROGRESS, THEY MAY NOT BE PROGRESSED.

WE HAD ACTUALLY ONE OF THE PROGRAMS THAT'S OUT IN THE PUBLIC DOMAIN WITH AN ADA-SCID, ADENOSINE DEAMINASE DEFICIENCY-BASED SEVERE COMBINED IMMUNODEFICIENCY, PROGRAM THAT CIRM HAS BEEN A BIG SUPPORTER OF OUT OF UCLA, DON KOHN'S PROGRAM. IT WAS SPUN OUT INTO A COMPANY, ORCHARD THERAPEUTICS, AS A LEAD CANDIDATE. BUT FOR CORPORATE REASONS, IT WAS NOT CONTINUED. THROUGH A VARIETY OF WAYS AND INFLUENCE THROUGH PATIENT ADVOCACY AND CIRM'S POLICY AS WELL AS WITH AGREEMENT FROM THE COMPANY, IT WAS

SENT BACK TO UCLA. THE IP WAS RETURNED SO THAT THE PROGRAM COULD CONTINUE. THAT'S BEEN REOPENED SO THAT IT CAN PROCEED AS AN ACADEMIC TRIAL.

NOW, THAT PROGRAM HAS DATA FROM JUST SHORT OF 50 PATIENTS CURED WITH MANY FOLLOW-UP STUDIES OF FIVE YEARS. IT'S INCREDIBLE. THEY'RE CURED OF THE FATAL IMMUNODEFICIENCY. SO VERY STRONG CLINICAL DATA, YET IT DOESN'T FIT INTO THE STANDARD MODEL OF HOW YOU COMMERCIALIZE THESE PRODUCTS.

SO WE DON'T HAVE ANY ANSWERS YET, BUT IT'S A VERY IMPORTANT PROBLEM STATEMENT FOR CIRM BECAUSE OUR ROLE IS TO DERISK PROGRAMS FOR UNDERSERVED DISEASES AND UNDERSERVED POPULATIONS THAT DON'T OFTEN FIT INTO THE STANDARD MODELS OF TODAY.

SO THE ACADEMIC CLINICAL TRIAL AND HEALTHCARE DELIVERY PROGRAMS, INCLUDING THE ALPHA CLINICS AND THE FUTURE COMMUNITY CARE CENTERS OF EXCELLENCE, HOPEFULLY WILL BE A WAY THAT WE CAN START TO MOLD A DIFFERENT MODEL WHERE THESE TYPES OF THERAPIES CAN GO FORTH, BUT WE DON'T HAVE THE ANSWER YET. THAT IS DEFINITELY ON OUR RADAR. AND MEANWHILE WE ARE SUPPORTING THE PROGRAMS THE BEST WE CAN SO THEY CAN STAY IN THE MIX, AND THEY CAN GAIN THE CLINICAL DATA AND MAKE THEIR WAY THROUGH THE DEVELOPMENT PATH AND REGULATORY APPROVAL.

DR. GOLDSTEIN: THANK YOU. THAT'S VERY HEARTENING.

DR. LOMAX: SO I THINK WE CAN TURN IT OVER TO SEAN BECAUSE, AGAIN, THERE'S SORT OF A THIRD LEG OF THIS TRIAD AND ANOTHER MAJOR OPPORTUNITY HE'S HERE TO DESCRIBE THIS MORNING.

DR. TURBEVILLE: CERTAINLY. SO WELCOME, EVERYBODY. I AM GOING TO ASK GEOFF PERHAPS TO MANAGE THE SLIDES IF THAT'S POSSIBLE OR PERHAPS MARIANNE. ALL RIGHT. WONDERFUL.

WELL, THANK YOU, EVERYBODY, MR. CHAIRMAN, AND OUR NOW CO-CHAIRMAN AND MEMBERS OF THE BOARD. THIS IS A FASCINATING DISCUSSION. MY NAME IS SEAN TURBEVILLE. I AM THE VICE PRESIDENT OF MEDICAL AFFAIRS. NEXT SLIDE PLEASE.

AND WE ARE ABOUT TEN MONTHS INTO THIS JOURNEY. WE ARE A SMALL GROUP. I HAVE TO SAY THAT THE STANDARD WORKING GROUPS, OF ALL THE WORKING GROUPS THAT WE ARE AFFILIATED WITH, REALLY EXCITED ABOUT THIS PROJECT SIMPLY BECAUSE IT DOES HAVE A LOT OF IMPACT ON CELL AND GENE THERAPIES, NOT NECESSARILY JUST WHEN WE TALK ABOUT CONSENT, BUT MORE IMPORTANTLY THERE'S LOT OF OF MARKETING REQUIREMENTS OF PATIENTS AND EVEN THE HEALTHCARE PROVIDERS THAT CERTAINLY THIS GROUP CAN GIVE US

GUIDANCE AS WE START TO DEVELOP PROGRAMS LOOKING INTO THE POSTMARKETING STAGE AS WELL.

SO AS I MENTIONED, THIS IS A NEW DEPARTMENT. THIS WAS BASED OFF DR. MARIA MILLAN'S VISION OF DEVELOPING A MEDICAL AFFAIRS AND POLICY GROUP THAT COULD START DEVELOPING OUTREACH PROGRAMS, RESEARCH THAT IS IN LINE WITH THE FIVE-YEAR STRATEGIC PLAN. WE ARE TASKED WITH NOT ONLY DEVELOPING THE ROAD MAP FOR THE ACCESS AND AFFORDABILITY, AND I KNOW THAT CAME UP EARLIER. I'LL TALK ABOUT THAT IN A FEW MINUTES. WE DO THAT IN COORDINATION WITH ANOTHER GROUP. THAT'S THE AAWG OR THE ACCESS AND AFFORDABILITY WORKING GROUP.

WE ARE ALSO RESPONSIBLE FOR POSTMARKETING RESEARCH, OUTCOMES, REGISTRIES, REAL-WORLD EVIDENCE, HEALTH ECONOMICS AND POLICY, HEOR, ETC., ALL THAT HAVE TOUCHPOINTS, OF COURSE, WITH THE STANDARDS WORKING GROUP.

WE HAVE FIVE MAJOR WORKSTREAMS THAT WE'VE KICKED OFF. GEOFF ALREADY MENTIONED THE ALPHA CLINICS THAT STARTED MANY YEARS AGO. AS HE MENTIONED, WE'RE NOW UP TO NINE CLINICS. THIS IS A GREAT OPPORTUNITY FROM A COLLABORATIVE GROUP WITH THE CENTERS OF EXCELLENCE. WE HAVE MANY IDEAS ON WHICH WE COULD PUT THINGS IN PLAY WITH RESPECT TO

POSTMARKETING REGISTRIES, COLLABORATIONS. THIS GOES BACK TO DR. LAWRENCE'S QUESTIONS ABOUT MAYBE PROGRAMS DRIVING SOME ASSETS THROUGH THE ALPHA CLINICS. SO LOTS OF IDEAS THAT I'LL TOUCH ON IN A FEW MINUTES.

THE OTHER WORKSTREAM IS THE ACCESS AND AFFORDABILITY WORKING GROUP. OF COURSE, THIS IS A CROSS-FUNCTIONAL GROUP THAT HAS LOTS OF EXPERTISE ALL THE WAY FROM, AND MANY OF YOU ARE ON THIS COMMITTEE, FROM PATIENT ADVOCACY TO THE CLINICAL TO THE OPERATIONS TO COMMUNITY. THIS IS A GROUP THAT WE PROVIDE INTEL AND GIVE FEEDBACK ON PROGRAMS THAT WE WANT TO PUT IN PLAY THAT HOPEFULLY WILL MEET OUR FIVE-YEAR STRATEGIC PLAN.

STANDARDS WORKING GROUP IS UNDER MEDICAL AFFAIRS. SO I AM LOOKING TO THIS GROUP TO GIVE US INSIGHT. THERE ARE SOME TOUGH QUESTIONS THAT ARE OUT THERE. THE WHOLE FIELD OF CELL AND GENE THERAPY, AS MANY OF YOU KNOW, PARTICULARLY ON THE GENE THERAPY SIDE, IS DEVELOPING, SORT OF THE BUILDING THE SHIP AS YOU SAIL IT, SO TO SPEAK. WE ARE LEARNING ABOUT THINGS THAT WE CAN BRING TO THE COMMITTEES AND HOPEFULLY THE COMMITTEE, THE STANDARDS WORKING GROUP, CAN GIVE US INSIGHT ON SOME OF THE POTHOLES AND SOME OF THE THINGS THAT YOU GUYS

ARE SEEING OUT THERE IN THE COMMUNITY.

THE OTHER IS THE COMMUNITY CARE CENTERS OF EXCELLENCE. AND THIS IS A BIG INITIATIVE. MARIA MILLAN JUST MENTIONED THIS. THIS IS WHERE WE'RE GOING OUTBOUND TO DEVELOP ORGANIZATIONS, CLINICS, IF YOU WILL, THAT WILL MEET THE DEMANDS OF THE RURAL COMMUNITY. WE'LL BE ABLE TO SUPPORT THE CLINICAL TRIALS IN THE CENTERS OF EXCELLENCE WITH RESPECT TO CELL AND GENE THERAPY. WE ALREADY KNOW, WE'VE DONE DUE DILIGENCE, YOU GUYS KNOW THIS, THAT THERE IS A BIG, BIG ROADBLOCK, IF YOU WILL, WITH RESPECT TO PATIENTS OUT THERE IN THE RURAL COMMUNITY WHO CANNOT GET TO THE CENTERS OF EXCELLENCE.

SO THE IDEA IS TO TAKE ALL THIS SUBJECT MATTER EXPERTISE, THE OPERATIONS, AND BRING THAT OUT TO THE COMMUNITY WITH A NUMBER OF COMMUNITY CARE CENTERS OF EXCELLENCE. IN FACT, THAT KICKED OFF LAST YEAR. WE NOW THIS MONTH HAVE A NEW WORKING SESSION THAT WILL BE HOSTED BY GEOFF IN THE RIVERSIDE AREA.

AND THEN FINALLY, IT'S THE PATIENT SUPPORT PROGRAM. THIS ISN'T ONE OF THE MAJOR PILLARS, BUT IT IS ONE OF THE STRATEGIES THAT SUPPORTS ACCESS AND AFFORDABILITY, AND I'LL TALK ABOUT THAT IN A FEW MINUTES.

THIS IS OUR TEAM. WE ARE A SMALL TEAM. THERE'S FOUR OF US RIGHT NOW. WE EXPECT TO GROW AS WE CONTINUE TO BUILD THE ORGANIZATION AND THE DELIVERABLES TO MEET THE FIVE-YEAR STRATEGIC PLAN.

A QUICK SHOUT-OUT TO EMILY REYES AND MARIVEL, WHO HAVE ONLY BEEN ON BOARD FOR LESS THAN SIX MONTHS AND HAVE REALLY HELPED US, ALONG WITH MARIANNE AND DOUG, TO GET US TO THE STARTING LINE TO ACTUALLY KICK THIS PROGRAM OFF AND OTHER PROGRAMS IN MEDICAL AFFAIRS. NEXT SLIDE.

ALL RIGHT. SO ONE OF THE FIVE-YEAR STRATEGIC PLAN THAT'S TO DEVELOP A ROAD MAP FOR ACCESS AND AFFORDABILITY. THIS IS A VERY INTERESTING, INTELLECTUALLY STIMULATING, CHALLENGING PROJECT. AS MANY OF YOU KNOW, MANY ORGANIZATIONS, PRIVATE AS WELL AS PUBLIC, ARE TRYING TO DEVELOP A ROAD MAP TO REDUCE COSTS, TO GIVE ACCESS TO PATIENTS. AND WE'RE DOING THE SAME THING. SO LAST MONTH WE KICKED OFF OUR ROAD MAP TO ACCESS AND AFFORDABILITY. THIS IS AN EXAMPLE OF WE'RE GOING TO START APPROACHING THIS ROAD MAP. THERE ARE A NUMBER OF STRATEGIES THAT WE PRESENTED TO THE AAWG THAT GAVE US THE BLESSING TO MOVE FORWARD. UNDER THOSE STRATEGIES WE HAVE A NUMBER OF TACTICS.

SO YOU WILL SEE MORE OF THIS AND PROBABLY

HAVE SEEN THIS IN THE PUBLIC DOMAIN EARLIER. WHAT WE'RE GOING TO BE FOCUSING ON FOR THE NEXT SIX TO SEVEN MONTHS WITH RESPECT TO ACCESS AND AFFORDABILITY IS, ONE, FACILITATE REIMBURSEMENT AND LIMIT PATIENT EXPENSES. THAT IS A STRATEGY THAT WE'RE GOING TO CONCENTRATE ON. WE HAVE OUR DUE DILIGENCE ON THE RESEARCH SIDE. THIS IS WHERE THE PATIENT SUPPORT SERVICES SITS TO GET ACCESS TO PATIENTS, AND I'LL TALK ABOUT THAT IN A FEW MINUTES. BUT WE ALSO HAVE A NUMBER OF STRATEGIES THAT WE'RE GOING TO BE PRESENTING TO THE AAWG ON A MONTHLY BASIS TO GIVE THEM A HEADS-UP IN TERMS OF WHAT WE LEARNED AND TO GET THEIR GUIDANCE ON WHETHER TO INCLUDE THAT IN OUR FINAL ROAD MAP TO THE ICOC.

AND IF YOU CAN IMAGINE WHAT WE'LL BE DOING FOR THE NEXT SIX MONTHS IS PRESENTING TO THE AAWG EACH ONE OF THESE STRATEGIES AND POTENTIAL TACTICS TO GET THEIR FEEDBACK AND INPUT.

SO ANOTHER STRATEGY WOULD BE TO SUPPORT NEW PAYER MODELS. MANY OF YOU HAVE PROBABLY WORKED IN GENE THERAPY OR FAMILIAR, FOR EXAMPLE, WITH THE VALUE-BASED CONTRACTS, WHICH ARE REALLY POPULAR RIGHT NOW. WE ARE NOW LEARNING ABOUT THESE. PRIVATE PAYERS ARE LEARNING ABOUT THESE. PUBLIC PAYERS ARE LEARNING ABOUT THESE. SO IT'S OUR

OPPORTUNITY TO UNDERSTAND WHAT THEY MEAN, HOW THEY IMPACT CALIFORNIANS, HOW THEY IMPACT OUR PAYER, AND HOW THEY IMPACT MEDICARE AND MEDICAID. AND SO WE'LL BE ABLE TO BRING SOME OF THAT INFORMATION BACK TO THE AAWG AND GIVE US GUIDANCE ON WHERE WE MIGHT BE ABLE TO MAKE AN IMPACT.

INTERESTING ENOUGH, MANY OF YOU MAY BE AWARE OF THIS, THAT ON THE EAST COAST FOR THE PRIVATE SECTOR THERE ARE ALREADY SMALL PAYERS THAT ARE STARTING TO COLLABORATE. THESE ARE CALLED RISK POOLS IN PREPARATION FOR THAT HIGH-END FRONT COST WHEN IT COMES TO THE GENE THERAPY.

INTERESTING ALSO ENOUGH, WHEN WE THINK ABOUT ACCESS TO CLINICAL TRIALS, THAT ROAD MAP CHANGES WITH RESPECT TO COMMERCIAL THERAPY. WHO IS THE UNMET NEED? WHO IS NOT GETTING ACCESS TO DRUGS? WHO'S GETTING ACCESS TO DRUGS QUICKER THAN OTHERS? THOSE ARE TWO SORT OF DIFFERENT LANDSCAPES, BUT WE'LL BE APPROACHING BOTH OF THOSE WITH POTENTIAL SOLUTIONS AND OPPORTUNITIES TO THE AAWG AS WELL AS THE ICOC.

ANOTHER STRATEGY THAT MANY OF YOU CAN PROVIDE GUIDANCE ON IS THE STATE POLICY ISSUES. SENATOR TORRES HAS ALREADY GOT US IN CONTACT WITH THE GOVERNOR'S OFFICE OF HEALTHCARE AND

AFFORDABILITY. IT'S A GREAT OPPORTUNITY FOR US TO DRIVE OUR ROAD MAP, HOPEFULLY ALIGNS WITH AND HAS SYNERGY WITH GOVERNMENT INITIATIVES IN TERMS OF HEALTHCARE AND AFFORDABILITY FOR THE STATE OF CALIFORNIA.

AND THEN FINALLY, WE WANT TO TALK ABOUT EXPAND THE CLINICAL INFRASTRUCTURE. SO THIS IS PIGGYBACKING OFF ALL THE GREAT WORK CIRM HAS DONE WITH RESPECT TO THE ALPHA CLINICS. DR. LAWRENCE, YOU MENTIONED EARLIER AN OPPORTUNITY. GEOFF MENTIONED HOW ROBUST THIS SYSTEM IS, THIS COLLABORATIVE GROUP. THERE'S A LOT OF UNTAPPED OPPORTUNITIES WITHIN THAT THAT WE MIGHT BE ABLE TO PRESENT TO THE ICOC IN TERMS OF EXPANDING ACCESS AND AFFORDABILITY, MORE IMPORTANTLY, ALSO ON THE RESEARCH SIDE. YOU THINK ABOUT PATIENT REGISTRIES WHICH ARE ABSOLUTELY CRITICAL FOR CELL AND GENE THERAPIES. WHEN WE THINK ABOUT CONSENT, FOR EXAMPLE, NO LONGER ARE WE JUST THINKING ABOUT CONSENT JUST FOR A PATIENT THAT'S ENROLLING INTO THE TRIAL, BUT VALUE-BASED CONTRACTS ARE VERY LONG. MEANING THERE'S EXPECTATIONS THAT THESE PATIENTS STAY IN THESE POSTMARKETING STUDIES FOR AN EXTENSIVE TIME. AND THAT'S IMPORTANT NOT ONLY FOR THE PAYERS, BUT ALSO FOR THE MANUFACTURERS. SO WE NEED TO HAVE

VALIDATED SYSTEMS WHERE WE CAN HELP COLLECT THAT INFORMATION AND HELP FACILITATE THAT FOR THE PATIENTS. SO THAT'S ANOTHER OPPORTUNITY.

LOTS OF IDEAS THAT WILL BE PRESENTED TO THE AAWG MOVING FORWARD, BUT I JUST WANT TO GIVE YOU A SNAPSHOT OF WHAT THAT ROAD MAP TO ACCESS AND AFFORDABILITY WOULD LOOK LIKE. NEXT SLIDE PLEASE.

NOW, WE KNOW THERE ARE MANY BARRIERS TO OVERCOMING AND TO ACHIEVING BROAD EQUITABLE ACCESS TO REGENERATIVE MEDICINE. MANY OF YOU HAVE SEEN THIS SLIDE BEFORE. WE HAVE DONE THE DUE DILIGENCE. THE LITERATURE AND THOUGHT LEADERS AND SUBJECT MATTER EXPERTS HAVE GIVEN US GUIDANCE. IF YOU DID DO A LITERATURE SEARCH, YOU WOULD FIND, CONSISTENT WITH WHAT WE REPORTED, THAT THERE'S CULTURAL AND SOCIAL DETERMINANTS, THERE'S INFORMATIONAL, THERE'S LOGISTICAL HURDLES, FINANCIAL, AND ABILITY BASED-HURDLES.

WHAT WE WANTED TO FOCUS WITH RIGHT OUT OF THE GATE WITH RESPECT TO A PATIENT SUPPORT PROGRAM IS IMPACT THE INFORMATIONAL, LOGISTICAL, AND FINANCIAL BARRIERS. THAT LEADS US INTO ONE OF OUR FIRST INITIATIVES, WHICH IS THE NEXT SLIDE. AND THIS IS CIRM'S PATIENT SUPPORT PROGRAM. SO AS I MENTIONED, AND MANY OF YOU ALREADY KNOW THIS, CELL

AND GENE THERAPY TRIALS ARE VERY DEMANDING ON PATIENTS AND THE HEALTHCARE PROVIDERS. AND THEY DO REQUIRE A LOT OF SUPPORT INTERNALLY, EXTERNALLY, FAMILY MEMBERS, THE PATIENTS, ET CETERA.

INTERESTING ENOUGH, IN THE LAST YEAR THERE'S BEEN PATIENT ASSISTANCE PROGRAMS THAT HAVE EMERGED TO ADDRESS THE BOTTLENECKS, WHETHER THEY'RE FINANCIAL, LOGISTICAL, ET CETERA, FOR PATIENTS THAT ARE INVOLVED IN THESE TRIALS. SO THE OBJECTIVE OF OUR PATIENT SUPPORT PROGRAM, WHICH WAS RECENTLY APPROVED BY THE AAWG AND THE ICOC, IS TO PROVIDE LOGISTICAL AND FINANCIAL SUPPORT TO PATIENTS SEEKING TO ENROLL IN OUR OTHER CLINICAL TRIALS WITH THE SPECIFIC AIM OF IMPROVING ACCESS, RETENTION IN CLINICAL TRIALS WITH AN EMPHASIS IN THE UNDERSERVED POPULATIONS. AND THIS PATIENT SUPPORT SERVICES IF YOU THINK ABOUT IT AS A HUB THAT HAS LOTS OF TOUCHPOINTS, NOT ONLY WITH THE ALPHA CLINICS, BUT POTENTIALLY ALSO WITH THE COMMUNITY CARE CENTERS OF EXCELLENCE.

SO THAT IS JUST ONE COMPONENT WITHIN THE LAST TEN MONTHS THAT WE'RE GETTING READY TO FLIP THE SWITCH. WE HAVE A LOT OF IDEAS WE WANT TO PRESENT AND EVEN BOUNCE OFF THIS GROUP THAT WILL HELP US PUT THINGS IN PLAY AND BE SUCCESSFUL. SO THIS IS JUST

ONE COMPONENT OF THE FIVE-YEAR STRATEGIC PLAN FOR THE ROAD MAP FOR ACCESS AND AFFORDABILITY.

AND WITH THAT, I WILL PAUSE AND SAY THANK YOU. AND I DO WANT TO THANK GEOFF FOR PUTTING THIS TOGETHER. THIS IS CERTAINLY HIS SWEET SPOT, AND HE'S BEEN DRIVEN TO GET THIS TO THE FINISH LINE OR AT LEAST THE STARTING LINE IN A SHORT AMOUNT OF TIME. SO I WANT TO THANK HIM AND THE REST OF THE MEDICAL AFFAIRS TEAM FOR PUTTING THIS IN PLAY. THANK YOU.

CO-CHAIRMAN KAHN: THANK YOU, SEAN. ANY QUESTIONS FROM THE -- I DON'T SEE ANY HANDS. DO YOU, GEOFF?

DR. LOMAX: I AM NOT SEEING HANDS AT THIS POINT. WE ARE COMING RIGHT UP ON THE TOP OF THE HOUR. SO MAYBE JUST GIVE EVERYONE THEIR BREAK, AND THEN WE'LL GET BACK INTO THE SESSION ON CONSENT CONSIDERATIONS WHICH IS FAIRLY EXTENSIVE.

CO-CHAIRMAN KAHN: SOUNDS GOOD. ALL RIGHT. THANKS, EVERYONE, FOR HANGING IN FOR THOSE FIRST TWO HOURS. WE HAVE A 30-MINUTE BREAK IS WHAT WE'RE DOING, GEOFF?

DR. LOMAX: CORRECT. 11:30 PACIFIC AND ADD HOURS ACCORDINGLY IF YOU'RE EAST OF US.

CO-CHAIRMAN KAHN: SOUNDS GOOD. WE'LL SEE

EVERYBODY IN A HALF HOUR.

(A RECESS WAS TAKEN.)

CO-CHAIRMAN KAHN: I MISSED THAT. I WASN'T CONNECTED. WHAT DID YOU JUST SAY?

DR. LOMAX: JUST SAYING SEEMS LIKE THE PEOPLE ENTERING HAVE SETTLED DOWN. WOULD YOU LIKE TO RECONVENE?

CO-CHAIRMAN KAHN: YEAH. SEEMS LIKE WE'RE ALL BACK. THANK YOU ALL FOR COMING BACK.

DR. LOMAX: SO THIS SEGMENT OF THE MEETING WE REALLY WANT TO HEAR FROM THE INVESTIGATORS. THEY'RE THE ONES THAT, I THINK, HAVE SOME OF THE MOST DIRECT INTERACTIONS WITH PATIENTS AND ARE DEALING WITH SOME OF THESE TREATMENTS. SO I WOULD LIKE TO TURN IT OVER TO DR. SHARMA WHO, BY THE WAY, I WOULD NOT AT ALL DESCRIBE YOU AS AN ARMCHAIR ETHICIST. I THINK FROM YOUR VANTAGE POINT YOU SIT IN A ROYAL CHAIR, AND SO I'M REALLY LOOKING FORWARD TO HEARING YOUR DISCUSSION OF THE ISSUES FROM YOUR PERSPECTIVE.

DR. SHARMA: THANK YOU, GEOFF. THAT'S VERY KIND OF YOU. ALLOW ME TO SHARE MY SCREEN. AND CAN SOMEBODY CONFIRM THAT YOU ARE SEEING THE CORRECT SCREEN?

DR. LOMAX: LOOKS RIGHT.

DR. SHARMA: SO I'M REALLY PRIVILEGED AND HONORED TO PART OF THIS GROUP AND TO BE ABLE TO PRESENT TO ALL OF YOU TODAY SOME OF OUR WORK AND SOME OF OUR THOUGHTS. AND I SORT OF MISCHIEVOUSLY CALLED THIS PRESENTATION "HOPE, HYPE, AND CURE: THE PROMISE AND PERILS OF GENETIC THERAPIES." AND YOU WILL SEE HOW THESE THREE FOUR-LETTER WORDS ARE INTRICATELY RELATED TO GENETIC THERAPIES AND ARE OFTEN CONFUSED BY EVERYBODY, INCLUDING CLINICIANS AND SCIENTISTS.

THESE ARE LIKE CONFLICTS OF INTEREST AND DISCLOSURES. I PARTICIPATE AS A PI ON SEVERAL CLINICAL TRIALS THAT ARE CONDUCTING GENE EDITING FOR SICKLE CELL DISEASE, AND I'M A CONSULTANT TO MANY OF THESE COMPANIES. NONE OF THIS WORK IS RELATED TO WHAT I'M PRESENTING TODAY. THOUGH I RARELY USE THE TERM "GENE THERAPY" TO ENCOMPASS GENE EDITING IN THIS TALK, AND I KNOW SOME FOLKS TAKE OFFENSE TO THAT, SO I APOLOGIZE IN ADVANCE, BUT FOR THIS TALK I DON'T THINK THAT'S VERY RELEVANT.

SO ONCE AGAIN, I'LL TALK ABOUT HOPE, HYPE, AND CURE AND HOW WE'VE ALL MISUSED AND CONFUSED THESE THREE TERMS. BEFORE THAT, I WANT TO BRIEFLY HIGHLIGHT WHAT THE PROBLEM IS. AND SO ONLY 5 PERCENT OF THE 7,000 KNOWN RARE DISEASES HAVE AN

APPROVED TREATMENT, AND HALF OF THESE RARE DISEASES ARE GENETIC IN ORIGIN. THEY PREDOMINANTLY AFFECT INFANTS AND CHILDREN. AND THESE DISEASES, THEY LEAD TO SIGNIFICANT ILLNESS AND EARLY DEATH IN THE INDIVIDUALS THAT THEY AFFECT. BECAUSE OF THESE, EVEN THOUGH THESE GENETIC DISEASES MAY OCCUR IN A VERY SMALL NUMBER OF POPULATION OF PATIENTS, COLLECTIVELY THEY ARE AFFECTING APPROXIMATELY 400 MILLION PEOPLE WORLDWIDE. AND THIS MAKES THESE RARE DISEASES, THE RARE GENETIC DISEASES, COLLECTIVELY ONE OF THE MOST UNDERSERVED COMMUNITIES IN MEDICINE TODAY AS THERE ARE HARDLY ANY APPROVED TREATMENTS FOR THEM.

AND SO THE FEW TREATMENTS THAT ARE CURRENTLY AVAILABLE, THEY TYPICALLY FOCUS ON DISEASE SYMPTOMS, AND THEY ARE UNABLE TO TAKE CARE OF THE UNDERLYING GENETIC CAUSE OF THE DISEASE. SO HEREIN LIES THE HOPE, WHICH IS AN EXPECTATION OF FULFILLMENT OF SUCCESS OR TO WANT SOMETHING TO HAPPEN. AND SO THE HOPE IS THAT THERE IS A POTENTIAL SOLUTION FOR THESE GENETIC DISEASES. AND I PUT POTENTIAL IN SORT OF APOSTROPHE COMMAS OVER HERE, WHICH YOU'LL UNDERSTAND WHY. WITH A BETTER UNDERSTANDING OF MODERN HUMAN GENETICS AND THE DEVELOPMENT OF NOVEL GENE MANIPULATION TECHNOLOGIES,

CRISPR CAS-9, ZINC FINGER NUCLEASES, GENETIC THERAPIES, THESE ARE THE NEXT FRONTIER IN OUR THERAPEUTIC DEVELOPMENT.

AND SO WITH ALL THESE ADVANCES IN SCIENCE, THERE IS A POTENTIAL THAT WE COULD ADDRESS THE UNDERLYING BIOLOGY OF MANY OF THESE GENETIC DISEASES. WE COULD REDUCE THE ONGOING NEED FOR TREATMENT FOR SYMPTOM CONTROL AND REDUCE THE BURDEN ON THE PATIENTS AS WELL AS THE HEALTHCARE SYSTEM BY USING THESE ADVANCES IN MODERN GENETICS AND GENE MANIPULATION TECHNIQUES.

AND INDEED OVER THE LAST TWO DECADES, WE HAVE SEEN A NUMBER OF MEDICATIONS WHICH HAVE UTILIZED THESE GENETIC TECHNIQUES, IMPROVED OUR UNDERSTANDING OF GENETICS OF THESE DISEASES WHICH HAVE LED TO THE DEVELOPMENT OF POTENTIALLY CURATIVE THERAPIES FOR A NUMBER OF THESE GENETIC DISEASES.

AND THIS IS WHERE THE HYPE COMES IN, WHICH IS PROMOTIONAL PUBLICITY OF AN EXTRAVAGANT KIND OR A CONTRIVED KIND. AND SO IN NOVEMBER OF 2021, S*CIENTIFIC AMERICAN* HAD THIS HEADLINE OF FOUR SUCCESS STORIES IN GENE THERAPY. THE FIELD IS BEGINNING TO FULFILL ITS POTENTIAL. AND THEN THE *NEW YORKER* SAID ARE WE ABOUT TO CURE SICKLE CELL DISEASE? AND WHEN THE *NEW YORKER* SAID SOMETHING,

THE *NEW YORK TIMES* COULDN'T STAY BEHIND. SO THEY OBVIOUSLY CAME FORWARD AND HAD THIS HEADLINE TALKING ABOUT "PIONEERING GENE THERAPY FREED HER OF SICKLE CELL DISEASE. IS A CURE AT HAND?" AND USED WORDS LIKE "EXTRAORDINARILY PROMISING," "CLINICAL TRIAL RESULTS HERE."

AND NOT JUST THESE LAY MEDIA JOURNALS, BUT ALSO AN ACADEMIC JOURNAL, WHICH IS THE OFFICIAL JOURNAL OF THE ROYAL PHARMACEUTICAL SOCIETY, THE "PHARMACEUTICAL JOURNAL," THEY HAD THIS EDITORIAL TALKING ABOUT "GENE THERAPY: FROM CATASTROPHE TO CURE IN 20 YEARS." AND THEN ANOTHER JOURNAL, "E-BIOMEDICINE," WHICH IS PROUDLY PUBLISHED BY THE LANCET GROUP, THEY CALL GENE THERAPY THE ULTIMATE CURE FOR HEREDITARY DISEASES. SO I THINK YOU WILL UNDERSTAND WHERE I'M GOING WITH ALL THIS.

ALL THESE HYPERBOLIC STATEMENTS IN LAY MEDIA OR IN ACADEMIC JOURNALS SIMPLY HYPE UP THE CURATIVE POTENTIAL OF THESE NOVEL MODALITIES. AND SO WHAT EXACTLY IS A CURE? SO WHEN I LOOK AT THE DICTIONARY, A CURE IS A COMPLETE OR A PERMANENT SOLUTION OR REMEDY TO RESTORE HEALTH, SOUNDNESS, OR NORMALITY AND TO RELIEVE A PERSON OF THE SYMPTOMS OF DISEASE OR A CONDITION.

AND SO THESE ARE THE WORDS WHICH I FIND

ARE IMPORTANT WHEN YOU'RE DEFINING A CURE. IT HAS TO BE A PERMANENT SOLUTION WHICH RESTORES COMPLETE HEALTH AND NORMALITY TO THIS PERSON OR PATIENT. AND WE'LL EVALUATE WHETHER THESE GENETIC THERAPIES, IF YOU'RE TALKING ABOUT AS CURATIVE, ARE ACTUALLY ACHIEVING THAT CURATIVE POTENTIAL OR NOT.

AND SO I AM A HEMATOLOGIST. I TAKE CARE OF CHILDREN WITH BLOOD DISORDERS. AND SO SICKLE CELL DISEASE IS ONE OF THOSE DISEASES WHICH I HAVE A LOT OF INTEREST IN, AND IT REMAINS THE FOCUS OF MY CLINICAL AND RESEARCH ENDEAVORS. SO I WANT TO TAKE EXAMPLE OF SICKLE CELL DISEASE AND WALK YOU THROUGH HOW THESE TREATMENTS HAVE BEEN DEVELOPED AND ARE THEY REALLY CURATIVE IN POTENTIAL. AND SO THIS WILL BE PROBABLY MY ONLY SLIDE TALKING ABOUT GENETICS.

SICKLE CELL DISEASE, IT'S CAUSED DUE TO A SINGLE POINT MUTATION IN THE HBB GENE, WHICH IS THE BETA-GLOBIN GENE, AND IT'S A SINGLE BASE REPLACEMENT FROM NORMAL GAG TO A GTG. AND WHAT THAT DOES IS IN THE PROTEIN SEQUENCE, INSTEAD OF GLUTAMIC ACID, THERE'S A VALINE PRESENT AT THE 6TH POSITION. AND NORMALLY HEMOGLOBIN MOLECULES ARE SUPPOSED TO BE TETRAMERS. THERE ARE FOUR PARTS WHICH COMBINE TOGETHER TO FORM THE HEMOGLOBIN MOLECULE. AND THEY ARE INSIDE ALL OF THE RED BLOOD CELLS WHICH ARE IN

OUR BLOOD. AND WHEN YOU HAVE A VALINE INSTEAD OF A GLUTAMIC ACID BECAUSE OF THIS MUTATION, THESE MOLECULES, THEY FORM LONG POLYMERS OR CHAINS.

AND THESE CHAINS ARE RESPONSIBLE FOR THE C SHAPE OR THE SICKLE SHAPE OF THE RED BLOOD CELLS. THESE RED BLOOD CELLS ARE HARD, THEY'RE STIFF, THEY GET STUCK IN BLOOD VESSELS. SO WHEREVER THEY GET STUCK IN THE DIFFERENT PARTS OF THE BODY, THEY CAUSE A PROBLEM. AND SO IF THEY GET STUCK IN THE BONES OR THE MUSCLES, THEY CAUSE BONE PAIN. IF THEY GET STUCK IN THE BRAIN, THEY CAN CAUSE STROKE. IF THEY GET STUCK IN THE CHEST, IN THE LUNGS, THEY CAUSE ACUTE CHEST SYNDROME AND SO FORTH AND SO ON. EVEN THOUGH IT'S A BLOOD DISORDER, SICKLE CELL DISEASE INDEED AFFECTS EVERY SINGLE ORGAN OF THE BODY.

NOT JUST THAT, BUT THE SYMPTOMS OF SICKLE CELL DISEASE, THEY PROGRESS WITH AGE. SO IN YOUNGER CHILDREN WE SEE SPLENIC SEQUESTRATION, STROKE. AS THE CHILDREN GET OLDER, THEY HAVE BONE DEATH, KIDNEY DAMAGE, COGNITIVE DYSFUNCTION. AND IN ADULTHOOD PATIENTS OFTEN DEVELOP BLOOD, LUNG, AND HEART PROBLEMS, ALL OF WHICH LEADS TO AN EARLY DEATH. AND MANY OF THESE THINGS THAT I HAVE HIGHLIGHTED IN RED OVER HERE ARE IRREVERSIBLE. ONCE PATIENTS DEVELOP THESE COMPLICATIONS, THERE IS NO GOING BACK. YOU

CANNOT FIX THEM. YOU CANNOT REVERT BACK TO NORMAL.

I ALSO WANT TO HIGHLIGHT THAT SICKLE CELL DISEASE DISPROPORTIONATELY AFFECTS INDIVIDUALS IN LOW AND MIDDLE INCOME COUNTRIES. THIS CARTOGRAM OVER HERE, I LIKE IT VERY MUCH. IT INFLATES THE SIZES OF THE DIFFERENT COUNTRIES BASED ON THE NUMBER OF NEWBORNS WITH SICKLE CELL DISEASE THAT THEY HAVE BORN EVERY YEAR. AND AS YOU CAN SEE, OUT OF THE 300,000 NEWBORNS BORN WITH SICKLE CELL DISEASE EVERY YEAR, THE MAJORITY ARE BORN IN NIGERIA AND INDIA AND THE REST OF THE SUB-SAHARAN AFRICA WHICH BEAR THE MAXIMUM BRUNT OF THESE DISEASES. AND THIS BECOMES IMPORTANT, AS I'LL TALK ABOUT IN THE LATER, COMPARING WHERE ALL THE CLINICAL TRIALS OF THESE DISEASES ARE BEING RUN CURRENTLY.

SO A CURE FOR SICKLE CELL DISEASE, IN MY OPINION, WOULD BE A PERMANENT SOLUTION WHICH RESTORES HEALTH AND NORMALITY, RELIEVING THE INDIVIDUAL OF ALL SYMPTOMS OF SICKLE CELL DISEASE AND ALSO TO BE ABLE TO GIVE EQUITABLE CONCERN AND ATTENTION TO SICKLE CELL DISEASE ALL OVER THE WORLD. SO THAT WOULD BE MY INTERPRETATION OF WHAT I WOULD CONSIDER A CURE FOR SICKLE CELL DISEASE TO BE.

WHEN YOU LOOK AT HAVE WE BEEN ACHIEVING THAT OBJECTIVE, PROBABLY NOT. HERE I'M LISTING THE

VARIOUS TREATMENTS WHICH ARE CURRENTLY AVAILABLE FOR SICKLE CELL DISEASE AND WHEN THEY WERE APPROVED. UNTIL FIVE YEARS AGO, THERE WAS ONLY ONE MEDICATION THAT WAS AVAILABLE FOR TREATMENT OF PATIENTS WITH SICKLE CELL DISEASE. OVER THE LAST FIVE YEARS, WHILE WE HAVE DEVELOPED MANY NEW MEDICATIONS, NONE OF THESE ARE CURATIVE. THESE MEDICATIONS HAVE TO BE TAKEN ON A REGULAR BASIS. THEY ONLY RELIEVE THE SYMPTOMS OF THE DISEASE, JUST LIKE I MENTIONED IN MY VERY FIRST SLIDE, AND THEY DON'T OFFER A PERMANENT AND LASTING CURE TO THESE INDIVIDUALS.

OF COURSE, BONE MARROW TRANSPLANT, WHICH WE HAVE KNOWN ABOUT THIS SINCE 1983, IT IS A POTENTIALLY CURATIVE TREATMENT, BUT YOU NEED TO FIND A DONOR, A WELL-MATCHED DONOR, TO PERFORM A BONE MARROW TRANSPLANT. AND THOSE DONORS ARE UNFORTUNATELY AVAILABLE FOR LESS THAN ONE-FIFTH OF ALL THE INDIVIDUALS WITH SICKLE CELL DISEASE WHO NEED A TRANSPLANT.

AND THEN HOPEFULLY GENE THERAPY MAY BE APPROVED EARLY THIS YEAR. I SHOULD PROBABLY UPDATE THIS SLIDE. I SHOULD CALL IT 2023. WE WERE HOPING THAT WE WILL GET APPROVAL BY LATE LAST YEAR, BUT IT DID NOT HAPPEN. HOPEFULLY GENE THERAPY WILL BE APPROVED IN EARLY 2023 BECAUSE THERE ARE MANY OF

THESE GENE THERAPIES WHICH ARE CURRENTLY IN DEVELOPMENT. SO ON THIS SLIDE I AM LISTING THE DIFFERENT METHODS BY WHICH WE CAN DO GENE THERAPY AND ALL THE DIFFERENT ACADEMIC CENTERS AND INDUSTRY, PHARMACEUTICAL COMPANIES THAT ARE PARTICIPATING IN DEVELOPING GENETIC THERAPIES. SO THIS IS A VERY RAPIDLY EVOLVING FIELD, AND THERE ARE A NUMBER OF COMPETITORS IN THIS FIELD. AND SO DEFINITELY THERE IS HOPE THAT WE WILL HAVE A POTENTIALLY CURATIVE THERAPY, HOPEFULLY MORE THAN ONE POTENTIALLY CURATIVE THERAPY SOON.

BUT THERE ARE -- THIS IS JUST NOT A PIPE DREAM. MANY OF THESE HAVE ACTUALLY BEEN ALREADY DONE. SO THERE ARE A NUMBER OF CASE REPORTS WHICH HAVE USED MANY DIFFERENT APPROACHES, CAS-9, LENTIVIRAL GENE ADDITION, SHRNA, WHICH HAVE ALREADY SHOWN PROMISE IN PATIENTS THAT HAVE RECEIVED THESE THERAPIES. SO WHEN I THINK OF THESE PATIENTS THAT HAVE ACTUALLY RECEIVED THESE GENETIC THERAPIES, A QUESTION COMES TO MY MIND. ARE THESE PATIENTS REALLY CURED, AGAIN IN INVERTED COMMAS. THESE PATIENTS CERTAINLY DON'T HAVE ANY SICKLE CELL ASSOCIATED PAIN CRISES AFTER THEY RECEIVED GENETIC THERAPIES. AND MOST OF THESE PATIENTS ARE ABLE TO DISCONTINUE EITHER TRANSFUSIONS OR OTHER MEDICATIONS

THAT THEY HAVE BEEN RECEIVING.

BUT I MENTIONED ALL THESE IRREVERSIBLE THINGS THAT PATIENTS CAN HAVE BECAUSE OF SICKLE CELL DISEASE, AND THESE DO NOT GO AWAY AFTER THESE PATIENTS HAVE UNDERGONE GENETIC THERAPIES.

SO MANY PATIENTS STILL NEED TO UNDERGO MULTIPLE ADDITIONAL PROCEDURES FOR MEDICAL MANAGEMENT OF THESE COMPLICATIONS THAT EITHER THEIR DISEASE CAUSED UP FRONT OR THE TREATMENT FOR THE DISEASE, WHICH IN THIS CASE GENE THERAPY CAUSED FOR THEM DURING THE COURSE OF THEIR TREATMENT. SO THESE PATIENTS HAVE TO KEEP UNDERGOING THAT TREATMENT.

I LIKE TO TELL MY PATIENTS, WHENEVER I'M TALKING TO THEM, THAT IF THEIR BODY IS LIKE A WALL, SICKLE CELL DISEASE IS LIKE A HAMMER. THE DISEASE KEEPS CHIPPING ON THEIR DISEASE EVERY SINGLE DAY OF THEIR LIFE UNTIL GENE THERAPY TAKES THE HAMMER AWAY, BUT GENE THERAPY DOESN'T REPAIR THE WALL ANY FURTHER. SO THE DAMAGE THAT'S BEEN DONE IS DONE. AND MANY OF THESE PATIENTS CONTINUE TO LIVE WITH THAT DAMAGE FOR THE REST OF THEIR LIVES.

SO I'M GOING TO SHARE TWO REPRESENTATIVE CASES, WHICH ARE VERY SIMILAR TO CASES THAT I'VE TAKEN CARE OF. I HAD THIS 21-YEAR-OLD BOY WITH SICKLE CELL DISEASE WHO WAS RECEIVING BLOOD

TRANSFUSION THERAPY FOR PAIN CRISES. AND THIS YOUNG MAN, HE NOW STARTED DEVELOPING RED BLOOD CELL ANTIBODIES SO COULD NOT GET BLOOD TRANSFUSIONS ANYMORE SO UNDERWENT GENE THERAPY ABOUT A YEAR AGO. AND SINCE HIS GENE THERAPY HAS NOT REQUIRED ANY MORE TRANSFUSIONS, DOES NOT HAVE SIGNIFICANT ACUTE PAIN ANYMORE, BUT HE CONTINUES TO HAVE CHRONIC PAIN, WHICH IS A KNOWN COMPLICATION OF SICKLE CELL DISEASE AND STILL REQUIRES OPIOID MEDICATIONS ALMOST ON A DAILY BASIS. HE STILL COMES AND SEES ME AND OUR PAIN MEDICINE PROVIDERS ON A VERY REGULAR BASIS.

THE SECOND CASE IS A 20-YEAR-OLD BOY WHO HAD A STROKE WHEN HE WAS A YOUNG CHILD. AGAIN, BECAUSE OF THE HISTORY OF STROKE, HE WAS RECEIVING BLOOD TRANSFUSIONS FOR STROKE PREVENTION. HE UNDERWENT GENE THERAPY ABOUT NINE MONTHS AGO AND NOW HAS NORMAL HEMOGLOBIN, DOES NOT NEED TRANSFUSIONS. BUT IS HE CURED? ARE THESE TWO PATIENTS THAT I JUST LISTED HERE, WILL THEY EVER BE CURED? IF THEY KEEP REQUIRING TREATMENTS, AND IF YOU GO BACK TO THE DEFINITION, WE SAID THAT CURE IS COMPLETE NORMALCY. ARE THESE CURED?

AND THE REASON I'M HYPING ON THIS THING SO MUCH IS THE WHOLE VOCABULARY AROUND THESE POTENTIALLY CURATIVE TREATMENTS, IT REVOLVES AROUND,

WHEN WE TALK TO OUR PATIENTS, WE TELL THEM THAT, HEY, IF YOU GET THIS TREATMENT, YOU WILL BE CURED. BUT SOMEWHERE IN THOSE 60-, 70-, 80-PAGE CONSENT DOCUMENTS, IT'S WRITTEN THAT THEIR SYMPTOMS MAY CONTINUE TO EVOLVE OVER TIME. THEY MAY NOT GO AWAY COMPLETELY, AND THEY MAY HAVE ADDITIONAL COMPLICATIONS BECAUSE OF THEIR GENETIC THERAPIES. AND SO I WANT TO TALK ABOUT WHAT ARE THE DIFFERENT CHALLENGES TO THE CURE, AND WE'LL COME BACK TO THIS CONSENT DOCUMENT DISCUSSION.

FIRST OF ALL, AS I MENTIONED, SOME OF THE ADVANTAGES OF AUTOLOGOUS GENE THERAPY OVER TRANSPLANTATION IS THAT NOT ALL PATIENTS HAVE A DONOR. SO FOR GENE THERAPY, A PATIENT CAN SERVE AS HIS OR HER OWN DONOR. AND SOME OF THE IMMUNOLOGICAL COMPLICATIONS THAT ARE ASSOCIATED WITH TRANSPLANTATION ARE NOT ASSOCIATED WITH GENE THERAPY. SO YOU DON'T HAVE TO WORRY ABOUT GRAFT VERSUS HOST DISEASE OR GRAFT REJECTION.

BUT AUTOLOGOUS GENE THERAPY, ESPECIALLY AUTOLOGOUS GENE THERAPY THAT INVOLVES EX VIVO MANIPULATION OF THE HEMATOPOIETIC STEM CELLS FOLLOWED BY INFUSION, STILL REQUIRES CONDITIONING OF THE PATIENTS USING CHEMOTHERAPEUTIC AGENTS. MOST COMMONLY USED CHEMOTHERAPY FOR CONDITIONING IS

BUSULFAN, WHICH WE USE FOR TREATMENT OF LEUKEMIA. AND BUSULFAN EXPOSURE CAUSES TEMPORARY HAIR LOSS, INFERTILITY, INCREASED RISK OF INFECTION, RISK OF DEVELOPING SECONDARY CANCERS DOWN THE LINE WHEN THAT RISK CAN BE PERSISTENT FOR ALMOST 15, 20 YEARS AFTER THESE PATIENTS HAVE UNDERGONE GENETIC THERAPY. ALSO A LOW, BUT A NON-ZERO RISK OF DYING DURING THE PROCESS OF GETTING GENE THERAPY.

SO GENE THERAPY, EVEN THOUGH IT COULD BE POTENTIALLY CURATIVE AND IT COULD POTENTIALLY TAKE AWAY THE WHOLE RISK OF COMPLICATIONS FROM SICKLE CELL DISEASE, THERE ARE ADDITIONAL RISKS THAT ARE INVOLVED ON THESE PATIENTS DURING THE PURSUIT OF THIS TREATMENT. AND THESE ARE JUST A FEW OF THEM. THERE ARE MANY OTHERS THAT WE EITHER DON'T ADEQUATELY TALK OR, EVEN IF WE TALK ABOUT THEM, I'M NOT A HUNDRED PERCENT SURE IF THE PATIENTS ACTUALLY LISTEN TO THAT BECAUSE, AS SOMEBODY MENTIONED A LITTLE WHILE EARLIER, BY THE TIME WE REACH TO THE CONSENT DOCUMENT, BY THE TIME WE REACH TO THAT DISCUSSION, THE PATIENT AND THE PHYSICIAN HAVE ALREADY MADE UP THEIR MIND. THEY ARE READY, THAT THIS IS WHAT THEY'RE GOING TO DO. SO ULTIMATELY ALL THAT 80-PAGE CONSENT DOCUMENT DOES THAT WE SIGN, IT'S A LEGAL REQUIREMENT WHICH I DON'T KNOW SERVES

ITS PURPOSE.

AND SO, AT LEAST AT OUR INSTITUTION, AND I KNOW OF MANY OTHERS, WE ALL BELIEVE THAT CONSENT DISCUSSIONS ARE AN ONGOING PROCESS WHERE, WHEN I MEET WITH A PATIENT, IT USUALLY IS AN HOUR, HOUR AND A HALF LONG DISCUSSION THAT HAPPENS PERHAPS FOUR OR FIVE TIMES BEFORE WE WILL ACTUALLY SIT DOWN WITH THE CONSENT DOCUMENT IN HAND. I MAY EVEN GIVE THE CONSENT DOCUMENT TO THE FAMILY AND ASK THEM TO READ IT AT THEIR LEISURE AT THEIR OWN TIME, BUT WE WOULD NOT OPEN THE CONSENT DOCUMENT AND LOOK AT IT UNLESS I HAVE HAD THESE MULTIPLE DISCUSSIONS WITH THE FAMILY, THE PATIENT AND THE FAMILY BOTH. BECAUSE I THINK SOME OF THESE NUANCES OF WHAT A CURE IS AND HOW A PATIENT'S LIFE MAY OR MAY NOT CHANGE AFTER UNDERGOING THESE REALLY COMPLICATING GENETIC THERAPIES, THIS CANNOT BE CONVEYED BY JUST READING THROUGH A DOCUMENT.

AND SO ONE OF THE CHALLENGES THAT WE HAVE ALSO SEEN WITH THESE GENETIC THERAPIES IS THAT MANY OF THESE GENETIC THERAPIES ARE EXTREMELY NEW. CRISPR-CAS9 WASN'T EVEN KNOWN UNTIL ABOUT 10, 15 YEARS AGO. AND SO MANY OF THESE TECHNOLOGIES THAT WE ARE USING ARE NEW, AND THEY COME WITH SOME UNKNOWN RISKS. AND SOME OF THESE UNKNOWN RISKS

BECAME EVIDENT IN 2021, FEBRUARY, WHEN ONE OF THE COMPANIES, BLUEBIRD BIO, WHICH WAS CONDUCTING A LENTIVIRAL GENE THERAPY APPROACH FOR GENE ADDITION OF SICKLE CELL DISEASE, IT ANNOUNCED THAT TWO OF THEIR PATIENTS HAD DEVELOPED A MYELOID MALIGNANCY. SUBSEQUENTLY EXTENSIVE INVESTIGATIONS WERE DONE, AND IT WAS SHOWN THAT THE LENTIVIRAL VECTOR WAS NOT RESPONSIBLE FOR DEVELOPMENT OF LEUKEMIA IN THESE TWO PATIENTS. WE COULDN'T CONCLUSIVELY SAY WHAT HAD HAPPENED OR WHAT CAUSED IT. IT IS POTENTIALLY POSSIBLE THAT PERHAPS THE UNDERLYING SICKLE CELL DISEASE THAT THESE PATIENTS HAD COULD HAVE PREDISPOSED THEM TO DEVELOPMENT OF LEUKEMIA. IT IS ALSO POSSIBLE THAT PERHAPS THE CELLULAR PROCESSING OR THE RECONSTITUTION THAT HAPPENED AFTER THEY UNDERWENT GENE THERAPY WAS RESPONSIBLE FOR EXPANSION OF CERTAIN CLONES THAT HARBORED A CERTAIN MUTATION, BUT ALL THAT IS VERY, VERY COMPLICATED.

IN THE END THIS IS -- IT'S A RISK THAT THESE PATIENTS TOOK WHILE THEY WERE PARTICIPATING IN A FIRST-IN-HUMAN CLINICAL TRIAL. OF COURSE, LONG-TERM FOLLOW-UP IS NEEDED SO THAT WE CAN ESTABLISH WHAT THE TRUE RISK OF THESE THERAPIES IS. WHAT I WANT TO HIGHLIGHT OVER HERE IS THAT THERE IS A LOT OF STUFF THAT WE DON'T KNOW ABOUT THESE NOVEL

TREATMENTS. AND SO IF WE DON'T KNOW ABOUT IT ADEQUATELY, HOW ARE WE GOING TO NOW COUNSEL OUR PATIENTS ABOUT THESE UNKNOWNS? AND ARE WE DOING A GOOD ENOUGH JOB IN OUR CONSENT DOCUMENTS?

THERE ARE SOME OTHER CHALLENGES WITH HEMATOPOIETIC STEM CELL GENE THERAPY, WHICH I'LL HIGHLIGHT BRIEFLY OVER HERE. OF COURSE, THERE ARE PROBLEMS ASSOCIATED WITH HEMATOPOIETIC STEM CELL COLLECTION, WHICH IS NOT AT ALL EASY. THERE ARE RISKS ASSOCIATED WITH OFF-TARGET EFFECTS. WE INTEND TO MODIFY A CERTAIN LOCATION IN THE GENOME, BUT COULD IT MODIFY SOMEWHERE ELSE? THERE ARE, OF COURSE, ISSUES WITH THE USE OF CHEMOTHERAPEUTIC AGENTS TO CONDITION THE PATIENTS BEFORE THEY RECEIVE HSC-BASED GENE THERAPY. SAFETY, AS I MENTIONED, ETHICAL CONCERNS, AND THEN FINANCIAL CONSIDERATIONS WHICH WERE ALSO RAISED EARLIER. AND LAST, BUT NOT THE LEAST, EQUITABLE ACCESS TO THESE THERAPIES. SO I'M GOING TO VERY BRIEFLY TALK ABOUT SOME OF THESE IN THE NEXT FEW SLIDES.

AND SO WHAT DO PATIENTS THINK ABOUT THESE GENETIC THERAPIES? SO WE CONDUCTED FOCUS GROUPS OF SICKLE CELL DISEASE PATIENTS TO ASK THEM QUESTIONS ABOUT WE ARE OFFERING THESE GENETIC THERAPIES IN OUR CLINIC AS A PART OF A CLINICAL TRIAL. AND, OF

COURSE, SOME OF THESE WILL BE APPROVED WITHIN THE NEXT FEW MONTHS. SO WE WANTED TO KNOW HOW MUCH DO PATIENTS KNOW ABOUT THESE THERAPIES, IF ANYTHING AT ALL. AND MAJORITY REPORTED NO OR VERY LITTLE KNOWLEDGE OF GENE THERAPY FOR SICKLE CELL DISEASE. AND ALMOST HALF OF THEM SAID THAT, IF THERE WAS ANY RISK OF CANCER FROM PARTICIPATING IN RECEIVING A GENE THERAPY, THAT THEY WOULD NOT ENGAGE IN THAT GENE THERAPY CLINICAL TRIAL.

AND SO AS I MENTIONED EARLIER, THERE WERE TWO CASES OUT OF 40 SOME PATIENTS WHO WERE TREATED. SO THAT RISK IS NOT MINIMAL. AND EVEN THOUGH THE LENTIVIRAL VECTOR WAS NOT INVOLVED DIRECTLY IN THE DEVELOPMENT OF CANCER IN THOSE PATIENTS, IT IS PLAUSIBLE THAT PERHAPS THE WHOLE PROCESS OF GENETIC MODIFICATION AND REINFUSION COULD HAVE HAD SOMETHING TO DO WITH IT. SO HALF OF OUR PATIENTS WOULD NOT EVEN PARTICIPATE IN THAT SORT OF THERAPY IF THERE WAS ANY RISK OF CANCER.

AND THERE'S ALWAYS THIS FEAR OF UNKNOWN VERSUS THE COMFORT WITH CURRENT THERAPY AMONGST ANY PATIENT POPULATION. THE TREATMENT-RELATED MORTALITY OF EITHER TRANSPLANTATION OR GENE THERAPY IS A KNOWN RISK WHICH CAN HAPPEN RATHER ACUTELY OVER A MATTER OF A FEW DAYS TO FEW WEEKS AFTER THESE PATIENTS

RECEIVE THE THERAPY. WHEREAS, EVEN THOUGH WE ALL KNOW THAT SICKLE CELL DISEASE REDUCES LIFE SPAN OF THESE INDIVIDUALS, THAT'S NOT A MORTALITY RISK THAT HAPPENS IN THE SHORT TERM. THESE PATIENTS WITH SICKLE CELL DISEASE WHO ARE DOING FINE TODAY CAN LIVE WITH THEIR SICKLE CELL DISEASE FOR DECADES, FOR 20, 30 YEARS BEFORE ORGAN DAMAGE CATCHES UP WITH THEM. SO THERE IS ALWAYS THAT DIFFICULTY TO ASSESS WHAT IS THE FUTURE RISK IN 20 YEARS VERSUS THE RISK OF PARTICIPATING IN A CLINICAL TRIAL TODAY?

LAST, BUT NOT THE LEAST, THESE THERAPIES ARE EXTREMELY COMPLICATED. AND THE HEALTH LITERACY OF MOST PATIENTS IS VERY LOW. SO HOW DO WE ADEQUATELY CONVEY SOME OF THESE RISKS AND CHALLENGES AND THE TECHNIQUES THAT WE CURRENTLY USE TO PERFORM THESE GENE THERAPIES TO OUR PATIENTS? I THINK THAT'S A TOPIC THAT ALL OF US ARE TRYING TO GRAPPLE WITH. AND SO I WANT TO HIGHLIGHT THIS ONE *60 MINUTE* CBS EPISODE THAT WAS AIRED A COUPLE OF YEARS AGO IN 2020.

SO THIS EPISODE WAS TALKING ABOUT THE LENTIVIRAL GENE THERAPY, AND A PATIENT AT NIH WHO HAD RECEIVED THAT THERAPY WAS HIGHLIGHTED IN THIS EPISODE. AND WHAT THE NARRATOR OF THE EPISODE SAID AS HE WAS DESCRIBING HOW THIS GENE THERAPY IS DONE,

THIS IS WHAT HE SAID. "HERE'S HOW IT WORKS. THE CORRECTED GENE SEEN HERE IN YELLOW IS INSERTED INTO THE HIV VIRUS. THEN BONE MARROW STEM CELLS ARE TAKEN FROM A PATIENT WITH SICKLE CELL ANEMIA. IN THE LABORATORY THOSE CELLS ARE COMBINED WITH A VIRUS CARRYING THAT NEW DNA."

AND SO FOR A LAYPERSON, FOR A PATIENT, ALL THAT STUCK IN THAT DISCUSSION WAS THE USE OF THE WORD "HIV VIRUS." NOW, WHAT IS TRUE IS THAT A LENTIVIRAL VECTOR IS INDEED A MODIFIED HIV VIRUS FROM WHICH ALL THE HIV CAUSING MACHINERY HAS BEEN REMOVED SO THAT VIRUS CANNOT PRODUCE HIV/AIDS. BUT NEVERTHELESS, THE USE OF THIS OVERSIMPLISTIC TERMINOLOGY OVER HERE, THAT THIS GENE THERAPY USES HIV VIRUS STUCK WITH A LOT OF MY PATIENTS AND OTHERS. SO MUCH SO THAT ONE OF OUR PATIENTS ACTUALLY CAME TO THE CLINIC WHEN ENROLLED ON A DIFFERENT GENE THERAPY TRIAL AND BASICALLY TOLD ME THAT, "FIRST, THEY GAVE US SYPHILIS AND NOW THEY'RE GIVING US HIV. I DON'T WANT TO PARTICIPATE IN THIS GENE THERAPY BUSINESS OF YOURS."

THERE IS ALSO A VERY PROFOUND MISTRUST OF MEDICAL PROFESSIONALS AND RESEARCH IN GENERAL. THIS IS ANOTHER STATEMENT THAT ONE OF OUR PATIENTS MADE WHEN THEY HEARD ABOUT THE ANNOUNCEMENT OF THESE

PATIENTS WHO HAD DEVELOPED LEUKEMIA ON THAT CLINICAL TRIAL. THIS PATIENT FLAT OUT ASKED US, "IS THERE SOMETHING NEW THAT YOU GUYS JUST LEARNED ABOUT, OR HAVE ALWAYS KNOWN THAT GENE THERAPY COULD CAUSE CANCER?"

AGAIN, AS I SAID, THE MESSAGING AROUND THESE NOVEL THERAPIES HAS BEEN PROBLEMATIC. IF WE USE THE HIGH FIVE TERMS LIKE CRISPR-CAS9, ZINC FINGER NUCLEASES, OBVIOUSLY NOBODY UNDERSTANDS THAT, BUT THEN WE MERELY SIMPLIFY IT AND JUST SAY THIS IS AN HIV VIRUS, THAT CAUSES EVEN MORE PROBLEMS. SO WHAT IS THE GOLDEN PART IN THE MIDDLE? HOW DO WE CONVEY THE RIGHT INFORMATION WHILE NOT MAKING IT TOO SIMPLE AND PROBLEMATIC?

AND SO GENE THERAPY IS INDEED HARD TO UNDERSTAND, AND THE LONG-TERM RISKS ARE CURRENTLY UNKNOWN. I THINK WHAT WE NEED TO DEVELOP ARE BETTER EDUCATIONAL MATERIALS AND WHAT I CALL INFORMED CONSENT 2.0 WHERE JUST A CONSENT DOCUMENT COMPRISING OF A BUNCH OF WORDS WRITTEN ON SHEETS AND SHEETS OF PAPER IS NOT THE WAY TO DO IT. I THINK POTENTIAL TRIAL PARTICIPANTS SHOULD BE ACTIVE PARTNERS AND STAKEHOLDERS IN THE DEVELOPMENT OF THESE THERAPIES AS WELL AS THE DEVELOPMENT OF THESE INFORMED CONSENT DOCUMENTS SO THAT THE DOCUMENTS ACTUALLY CONTAIN THE

INFORMATION THAT THE PATIENTS ACTUALLY WANT TO KNOW, THAT THEY CARE ABOUT. AND COULD WE JUMP BEYOND THESE DOCUMENTS AND DEVELOP ACTUALLY AUDIOVISUAL AIDS WHICH THE PATIENTS ARE ABLE TO THEN ENGAGE WITH AND LOOK THROUGH OR READ OR LISTEN TO AT THEIR OWN LEISURE AND LEARN ABOUT THESE THERAPIES AT THEIR OWN PACE?

AND SO I THINK DEVELOPMENT OF THESE EDUCATIONAL MATERIALS, WE ABSOLUTELY HAVE TO GET INPUT FROM PATIENT REPRESENTATIVES AND ADVOCATES SO THAT WE DON'T DEVELOP A THERAPY THAT IN THE END NOBODY WANTS.

THERE ARE ALSO CONCERNS ABOUT WHO'S ELIGIBLE TO PARTICIPATE IN THESE CLINICAL TRIALS. THE PHARMACEUTICAL COMPANIES AND ACADEMIC CENTERS ALIKE, WE PUT THESE VERY RIGID BOOKMARKS AROUND THE ELIGIBILITY, THAT YOU HAVE TO MEET THIS CRITERIA TO BE ELIGIBLE FOR A CLINICAL TRIAL. BUT THEN THESE THERAPIES GO OUT AND ARE AVAILABLE TO PATIENTS ONCE THEY ARE APPROVED WHO DO NOT FIT THAT MOLD. AND HOW THESE AFFECT THOSE PATIENTS, IT'S AN AREA THAT IS A COMPLETE BLACK BOX THAT WE DON'T KNOW ABOUT.

ALSO, WE WANT TO ENROLL CHILDREN AS QUICKLY AS POSSIBLE BECAUSE WE BELIEVE THAT CHILDREN, BEFORE THEY DEVELOP ALL THE COMPLICATIONS

RELATED TO THESE DISEASES, WOULD BE THE PERFECT CANDIDATES FOR RECEIVING THESE THERAPIES. BUT HOW EARLY IS TOO EARLY AND WHO GETS TO DECIDE THAT? IS TREATMENT OF THREE ADULTS ENOUGH? OR DO WE NEED DATA ON 12 ADULTS OR 20 ADULTS? HOW MANY ADULT PATIENTS NEED TO BE TREATED ENOUGH FOR A CHILD TO RECEIVE THAT?

AGAIN, I'M GOING TO SKIP THIS IN THE INTEREST OF TIME. I THINK I'VE SPOKEN ENOUGH ABOUT THIS. BUT, AGAIN, WHAT I'M TRYING TO REFLECT OVER HERE IS THAT SOME OF THESE HARD RULES THAT WE CREATE AROUND CLINICAL TRIAL ENROLLMENT MAY NEED TO BE THOUGHT OVER AGAIN SO THAT WE ACTUALLY PROVIDE THE MOST OPPORTUNITY FOR BENEFIT TO OUR PATIENTS WHILE MAINTAINING THESE SAFEGUARDS AROUND THESE NOVEL THERAPIES.

AND THEN THERE ARE, OF COURSE, CONCERNS ABOUT FINANCIAL IMPLICATIONS. GENE THERAPIES, AS YOU ALL KNOW, ARE ONE OF THE MOST EXPENSIVE TREATMENTS EVER DEVELOPED. ZYNTEGLO, WHICH IS THE LENTIVIRAL GENE THERAPY FOR SICKLE CELL DISEASE AND THALASSEMIA, WAS PRICED AT $1.8 MILLION IN THE EUROPEAN UNION WHEN IT WAS APPROVED THERE. AND THE COMPANY WHICH WAS MANUFACTURING THIS DRUG JUST PULLED OUT OF EU, CITING THAT EU SAID THAT THEY

WOULD PAY $900,000, AND THE COMPANY BASICALLY SAID THAT THAT'S TOO LOW AND THEY WOULD NOT BE ABLE TO MANUFACTURE THIS TREATMENT. EVEN THOUGH THIS THERAPY WAS APPROVED IN THE EUROPEAN UNION ALMOST TWO, THREE YEARS AGO, NO PATIENT HAS ACTUALLY RECEIVED ACCESS TO THIS THERAPY THERE YET.

AND ZYNTEGLO WAS RECENTLY APPROVED IN THE U.S., AND I'VE SEEN MULTIPLE REPORTS. I THINK THERE WAS ONE REPORT THAT SAID IT COULD BE PRICED AT $2.6 MILLION, BUT DEFINITELY IT'S MORE THAN $2 MILLION APIECE. AND SO THAT'S A VERY HIGH SUM FOR PATIENTS IN A DEVELOPED COUNTRY. I DON'T KNOW HOW PATIENTS IN LOWER AND MIDDLE INCOME COUNTRIES WHERE I SHOWED YOU THIS CARTOGRAM PREVIOUSLY, HOW ARE ANY OF THE PATIENTS IN AFRICA AND INDIA EVER GOING TO BE ABLE TO AFFORD THIS TREATMENT IF IT COSTS $2 MILLION IN THE U.S. AND IT'S NOT AVAILABLE FOR PEOPLE IN THE EUROPEAN UNION EITHER?

SO WHAT, IF ANY, PAYMENT MODELS WOULD BE APPLICABLE TO THESE THERAPIES? WHAT IF THERE'S NO RESPONSE TO THE THERAPY? OR IF THE RESPONSE WEARS OFF, WOULD THE PATIENTS GET THEIR MONEY BACK? AND HOW WOULD SELF-FINANCING OR UNINSURED PATIENTS, WHICH UNFORTUNATELY ARE THE MAJORITY OF PATIENTS IN THE WORLD, HOW WOULD THEY BE ABLE TO EVER AFFORD

THESE THERAPIES ARE QUESTIONS WHICH ARE BEYOND THE REACH OF MOST OF THE ACADEMICS.

AND SO IS THE CURE ACCESSIBLE TO INDIVIDUALS WHO NEED IT THE MOST? I WOULD ARGUE THAT, WHILE MANY LOW AND MIDDLE INCOME COUNTRIES CURRENTLY DO NOT HAVE THE CAPACITY TO DELIVER THESE THERAPIES BECAUSE THESE ARE SO COMPLICATED AND THERE ARE OTHER COMPETING PRIORITIES LIKE NUTRITION, HIV, MALARIA, MANAGEMENT OF THOSE DISEASE IS MUCH MORE IMPORTANT THAN TAKING CARE OF SICKLE CELL DISEASE OR OTHER HEMOGLOBINOPATHIES IN THESE COUNTRIES. I DO THINK THAT THERE IS AN OPPORTUNITY TO LEAP FROG INTO GENE THERAPY IN THESE LOW AND MIDDLE INCOME COUNTRIES AND SKIP TRANSPLANTATION COMPLETELY BECAUSE, FIRST OF ALL, EVEN THOUGH GENE THERAPY OR GENE EDITING IS COMPLICATED, IT IS INDEED A LITTLE LESS COMPLICATED FROM A DELIVERY STANDPOINT THAN TRANSPLANTATION. THE MONITORING IS RATHER EASIER. THERE ARE LESS LOGISTICAL CHALLENGES SURROUNDING IMMUNOSUPPRESSION, ET CETERA.

AND SO I WOULD EVEN ARGUE THAT IN LOW AND MIDDLE INCOME COUNTRIES WHERE ACCESS TO OTHER COMPLICATED THERAPIES OR EVEN DRUG THERAPIES, WHICH ARE VERY EXPENSIVE, IS JUST UNAFFORDABLE OR NOT EASILY AVAILABLE, AND MONITORING OF THESE PATIENTS

WITH THESE DISEASES IS SO COMPLICATED. GENE THERAPY MIGHT ACTUALLY BE THE AVENUE THAT WE CAN PURSUE IN THESE COUNTRIES AND LOW RESOURCE SETTINGS.

AND SO TO SUMMARIZE, I WOULD SAY THE LONG-TERM SAFETY AND RISKS OF NOVEL THERAPIES, THEY NEED TO BE ESTABLISHED. OF COURSE, THE CLINICAL TRIALS AND LONG-TERM FOLLOW-UP ARE GOING ON RIGHT NOW. OVERCOMING THE COST BARRIER IS CRUCIAL TO IMPROVING ACCESSIBILITY TO THESE THERAPIES. AND WE HAVE TO REMEMBER WHERE ARE THE PATIENTS WHO NEED THESE THERAPIES THE MOST? WHAT IS THE GLOBAL BURDEN OF THESE DISEASES? AND PATIENT-CENTERED AND CULTURALLY COMPETENT EDUCATIONAL MATERIAL IS CRITICAL FOR THE DISSEMINATION OF THESE THERAPIES. AND ENGAGING WITH PATIENTS AS PARTNERS FROM THE VERY BEGINNING TO DEVELOP MEANINGFUL CURES IS MOST IMPORTANT.

AND SO THERE IS HOPE THAT MANY OF THESE GENETIC DISEASES MIGHT HAVE A TREATMENT SOON WITH THE HELP OF NOVEL GENOME EDITING METHODS AND DEVELOPMENT OF GENETIC THERAPIES. THERE'S ALSO A HYPE THAT MOST OF THESE TREATMENTS ARE POTENTIALLY CURATIVE. I WOULD ARGUE THAT THEY ARE NOT. THEY ARE POTENTIALLY CURATIVE IN MOST OF THE PATIENTS, BUT NOT EVERYBODY. AND SO WE HAVE TO BE CAREFUL

AROUND THE WORDS THAT WE USE. AND, OF COURSE, LONG-TERM FOLLOW-UP IS NEEDED TO ESTABLISH BOTH SAFETY AS WELL AS THE CURATIVE POTENTIAL. BUT CURE WILL NEED TO BE DEFINED INDIVIDUALLY FOR EACH PATIENT AND FOR EACH DISEASE AND MAY NOT BE THE SAME FOR EVERY SINGLE PATIENT. LIKE I MENTIONED, SOME OF THESE PREEXISTING ORGAN FUNCTION DEFICITS, THEY MAY CONTINUE TO NEED MEDICAL ATTENTION BEYOND THE HEMATOLOGICAL OR CURE AS WE DEFINE OTHERWISE.

SO WITH THAT, I DO WANT TO THANK A LOT OF FOLKS WHO HELP ME IN COLLECTING SOME OF THIS DATA AND ANALYZING THESE THOUGHTS THAT I COULD PRESENT TO YOU TODAY. OF COURSE, MANY OF OUR FUNDING SOURCES. I'LL BE HAPPY TO TAKE ANY QUESTIONS NOW DURING THE DISCUSSION. OR IF I'M UNABLE TO TAKE THEM, THIS IS MY EMAIL ADDRESS. AND I ALSO TWEET ABOUT THESE GENETIC THERAPIES OF SICKLE CELL DISEASE ON TWITTER, THOUGH I UNDERSTAND THAT'S NOT THE PREFERRED SOCIAL MEDIA PLATFORM ANYMORE. IF YOU ARE STILL THERE, WE CAN ENGAGE ON THAT TOO. SO THANK YOU SO MUCH FOR YOUR ATTENTION, AND I'LL BE HAPPY TO TAKE ANY QUESTIONS NOW.

CO-CHAIRMAN KAHN: HANDS? I CAN START. CAN YOU ALL HEAR ME?

DR. SHARMA: YES.

CO-CHAIRMAN KAHN: GOOD. THANK YOU FOR THAT. AND NOTING THAT MY COLLEAGUE, YORAM UNGURU, IS ONE OF THE PEOPLE WHO WAS ON YOUR LAST SLIDE. SO I'VE HAD A LITTLE BIT OF CONVERSATION ABOUT SOME OF THESE TOPICS WITH HIM.

I WONDER IF YOU COULD -- TWO THINGS. WONDER IF YOU CAN SAY SOMETHING ABOUT THE RECRUITMENT PROCESS AND HOW SUCCESSFUL OR NOT IT HAS BEEN. SO OBVIOUSLY THERE'S EXPERIENCE WITH CONSENT IN THESE VERY COMPLICATED CONTEXTS THAT YOU HAVE UNDERTAKEN IN THE CLINICAL TRIAL CONTEXT. AND WONDERING IF THERE HAS BEEN ANY PARTICULAR SETS OF CHALLENGES, ISSUES WITH RECRUITMENT, OR HAS IT BEEN EASY TO FILL THESE TRIALS? SO THAT'S ONE. GO AHEAD. I'LL ASK MY SECOND AFTER YOU ANSWER THAT.

DR. SHARMA: WELL, FORTUNATELY OR UNFORTUNATELY, MOST OF THE EARLY PHASE CLINICAL TRIALS RECRUIT A VERY SMALL NUMBER OF PATIENTS. SO MOST OF THESE TRIALS ARE OPEN AT, LET'S SAY, 15 CENTERS WORLDWIDE. AND EACH CENTER RECRUITS MAYBE TWO OR THREE PATIENTS BECAUSE THE TOTAL GLOBAL RECRUITMENT IN THESE TRIALS IS MAYBE ABOUT 45 TO 50, 60 PATIENTS ANYWAY.

SO WHEN YOU LOOK AT THAT, WE ARE TREATING A VERY, VERY SMALL NUMBER OF PATIENTS IN THESE

CLINICAL TRIALS. AND THAT'S THE BASIS OF THESE DRUG THERAPIES, CELLULAR THERAPIES, GETTING APPROVAL. AND SO I'D SAY RECRUITING ONE OR TWO PATIENTS HAS NOT BEEN THAT CHALLENGING.

HAVING SAID THAT, I HAVE SOMETIMES HAD TO DISCUSS THESE THERAPIES WITH ALMOST SIX TO SEVEN PATIENTS TO FILL UP ONE SLOT. AND SO IT'S A DOUBLE-EDGED SWORD THAT YOU DON'T HAVE TO RECRUIT TOO MANY PATIENTS ON THESE CLINICAL TRIALS, SO IT'S NOT THAT HARD. BUT EVEN TO FILL UP THAT ONE SPOT, YOU HAVE TO DISCUSS THE THERAPY WITH MANY, MANY MORE.

IT'S GENERALLY A LITTLE BIT HARDER IN THE BEGINNING WHEN THERE IS NO DATA; BUT ONCE A COUPLE OF PATIENTS HAVE BEEN TREATED AND THERE ARE EARLY CLINICAL TRIAL RESULTS, AND I'M SURE, AS YOU WILL NOTICE, THESE PHARMACEUTICAL COMPANIES, EVEN WHEN THEY HAVE TREATED JUST ONE OR TWO PATIENTS AND THEY HAVE MAYBE LIKE A SIX-MONTH FOLLOW-UP, THEY MAKE A BIG NEWS AND A BIG ANNOUNCEMENT ABOUT IT, WHICH IS THE HYPE THAT I MENTIONED ABOUT. THEY TALK ABOUT IT AT ACADEMIC CONFERENCES AND THEY MAKE A PRESS RELEASE, AND THERE'S A LOT OF HOOPLA AROUND IT.

AND SO THAT SORT OF PUBLICITY DOES MAKE IT A LITTLE BIT EASIER TO RECRUIT PATIENTS, BUT I ALSO

WORRY THAT THAT ALSO CREATES SOME OF THIS THERAPEUTIC MISCONCEPTION AND AN EXPECTATION OF CURE THAT, HEY, THIS IS A TREATMENT THAT, IF I GET THAT, I'LL ABSOLUTELY BE CURED OF MY DISEASE, WHICH IS, AS WE ALL KNOW, THAT THERE IS ALWAYS A STATEMENT IN ANY PHASE 1 CLINICAL TRIAL THAT WE DON'T KNOW IF THIS TREATMENT WILL EVER WORK FOR YOU OR NOT. BUT I THINK MOST OF US, INCLUDING CLINICIANS AND PATIENTS, THEY CONSIDER THAT STATEMENT TO BE JUST LEGAL JARGON AND MOVE ON, BUT THAT'S NOT THE CASE.

THERE IS A VERY LIKELY POSSIBILITY THAT SOME OF THESE PHASE 1 THERAPIES MAY NOT WORK. SO THAT'S WHY I THINK THERE IS A TUSSLE BETWEEN THE HYPE AND THE POTENTIALLY CURATIVE POTENTIAL OF THESE THERAPIES. SO YEAH. THAT WAS A LONG-WINDED WAY TO ANSWER YOUR QUESTION, BUT I WANTED TO GET ALL OF THESE THINGS OFF MY CHEST.

CO-CHAIRMAN KAHN: I'M HAVING A COMPUTER ISSUE. MAYBE SOMEONE ELSE CAN TAKE OVER FOR THE MOMENT. I DON'T KNOW IF YOU CAN HEAR ME.

CO-CHAIRMAN FISHER: WE CAN HEAR YOU, AND I CAN TAKE OVER. I DON'T KNOW YOUR FIRST NAME.

DR. WAGNER: SO THIS IS JOHN WAGNER. SO THE ONE THING, AS YOU WERE SPEAKING, THAT OCCURS TO ME, THINK ABOUT THE EXPERIENCE PARTICULARLY AT ST.

JUDE, BUT ALL OF US WHO DO PEDIATRIC ONCOLOGY AND HOW THAT'S EVOLVED OVER TIME. BUT ALSO, AS YOU KNOW, PARTICULARLY AT ST. JUDE AND A FEW OTHER PLACES, WE HAD NO IDEA THE KINDS OF LATE EFFECTS THAT WE WOULD SEE IN THE FUTURE, BUT THAT WAS 20, 30 YEARS DOWN THE ROAD.

SO THERE ARE THINGS THAT WE CANNOT FORESEE. AND I THINK THERE ALSO NEEDS TO BE IN SOME WAYS, AT LEAST FROM OUR POINT OF VIEW, AND IT'S DIFFERENT FROM OUR ACADEMIC POINT OF VIEW VERSUS WHAT THE PATIENTS HEARS OR THINKS; BUT AS YOU SAY, WHEN WE TALK ABOUT THE FIRST SUCCESS, THE TYPICAL FIRST PHASE 1 STUDY IS REALLY LOOKING AT A SPECIFIC ENDPOINT THAT IS NOT CURE. EVEN IN THE PHASE 2 STUDY, YOU'RE LOOKING FOR EARLY ENDPOINTS.

AND SO ALL OF THE SUCCESS AND HOOPLA AND EXCITEMENT ABOUT IT WAS REALLY AROUND THE EARLY RESULTS THAT ACHIEVED, AND LET'S SAY IT WAS IN TERMS OF ENGRAFTMENT OR YOUR PROPORTION OF SICKLE CELLS OR LACK OF. AND SO THAT'S WHERE THE EXCITEMENT COMES FROM BECAUSE IF YOU DON'T GET THAT, YOU CAN'T GET TO THE LONG-TERM RECOVERY.

I THINK THAT WHAT YOU'RE GOING AFTER IS THAT SOMEHOW WE HAVE TO DO BETTER ABOUT CLEARLY DELINEATING THE EARLY ENDPOINTS VERSUS WHAT THE

LONG-TERM EXPECTATION IS. REALLY IN A PHASE 1-2 STUDY, PARTICULARLY A PHASE 1, EFFICACY REALLY SHOULD BE PLAYED DOWN MORE THAN IT IS, BUT EFFICACY MEANS DIFFERENT THINGS TO DIFFERENT PEOPLE. OF COURSE, CURE IS WHAT YOU'RE LOOKING FOR.

THE OTHER THING, AS YOU KNOW, IN MORE RECENT YEARS, A COUPLE YEARS AGO I DID A STUDY WITH THE CIDMTR. AND WE FOR THE FIRST TIME EVER LOOKED AT WHAT HAPPENED TO SICKLE CELL PATIENTS 20, 25 YEARS DOWN THE ROAD. WHAT WAS SHOCKING TO ME IS THAT NO ONE HAD EVER DONE THAT STUDY. WHAT WE HAD SEEN IS WITH REDUCED INTENSITY CONDITIONING, GRAFT FAILURE NEVER STOPPED. THE PATIENTS, THE LONGER THEY WENT OUT, BUT YET ALL THE REPORTS SAID 10 PERCENT GRAFT FAILURE, BUT THEY TYPICALLY STOPPED AT TWO YEARS. BUT IF YOU GO ON BEYOND THAT, IT NEVER STOPPED. PATIENTS CONTINUED TO FAIL TO ENGRAFT.

THE OTHER THING WE LEARNED DURING THAT PERIOD OF TIME WITH THE AMERICAN SOCIETY OF HEMATOLOGY WAS THAT THE VERY REASON FOR WHICH THE SICKLE CELL PATIENT WENT TO TRANSPLANT WAS NOT FOLLOWED THE SAME WAY AFTER TRANSPLANT OR EVEN REPORTED. SO IF YOU WENT IN FOR PAIN CRISES, WHAT HAPPENED TO THE PAIN CRISES AFTER TRANSPLANT? OR IF YOU WENT IN FOR CHEST SYNDROME, WHAT HAPPENED TO

THAT AFTER TRANSPLANT? WHATEVER THE INDICATION WAS FOR TRANSPLANT, THAT WAS NOT REPORTED.

SO PART OF -- WE HAVE A NUMBER OF DIFFERENT ISSUES HERE. ONE IS THAT THE ONLY WAY WE CAN LEARN IS BY MAKING SURE THAT CERTAIN WAYS OF REPORTING ARE DONE. AND THIS OBVIOUSLY INFLUENCES US WHEN WE THINK ABOUT THE GRANTS WORKING GROUP AND HOW THEY SEE THE TRIALS. BUT ALSO WE HAVE TO THINK ABOUT HOW IT'S PRESENTED TO OUR PATIENTS. AND PERHAPS, AS WE TALK IN THE FUTURE ABOUT THE DESIGN OF CONSENT PROCESSES, THIS MIGHT BE PART OF THAT.

BUT SOME OF THESE UNKNOWN RISKS, REMEMBER, SOME OF IT WAS, FOR EXAMPLE, CLONAL HEMATOPOIESIS. THAT WHOLE FIELD WAS EVOLVING AT THE SAME TIME YOU WERE STARTING THE GENE THERAPY TRIALS. SO GOT TO KEEP THAT IN MIND TOO, THAT THE FIELD IS EVOLVING IN MANY DIFFERENT ASPECTS, AND WE COULDN'T HAVE PREDICTED HOW THAT WOULD IMPACT OUR STUDY EVEN THOUGH IT'S NOT REALLY PART OF OUR STUDY. ANYWAY, IT'S MORE OF A COMMENT THAN ANYTHING ELSE.

DR. SHARMA: YOUR POINT IS WELL TAKEN, DR. WAGNER. I COMPLETELY AGREE WITH YOU. BUT I THINK WHAT I'M TRYING TO ALLUDE TO, AND I THINK YOU DID THAT VERY WELL AS WELL, FOR MANY OF THESE PHASE 1 STUDIES, THE ENDPOINT IS A CERTAIN BIOMARKER, LET'S

SAY HEMOGLOBIN OR NUMBER OF ADVERSE EVENTS. UNFORTUNATELY, THE WAY THESE RESULTS ARE USUALLY PRESENTED, EITHER AT ACADEMIC CONFERENCES OR IN PRESS RELEASES AND THE WAY THEY ARE DISSEMINATED, THE WORD "CURE" GETS THROWN AROUND A WHOLE BUNCH. AND THEN HOW THAT MESSAGING SPREADS IN SOCIAL MEDIA OR IN PATIENT NETWORKS IS COMPLETELY DIFFERENT FROM HOW IT IS INTENDED TO BE SHARED.

AND SO I THINK THOSE ASPECTS ARE THE ONES THAT NEED TO BE CAREFULLY CRAFTED AND DISCUSSED. AND AT THE SAME TIME, I UNDERSTAND, AND I'M WITH YOU COMPLETELY, THAT SOME OF THESE LATE EFFECTS AND PROBLEMS THAT WE HAVE SINCE IDENTIFIED, WE DIDN'T EVEN KNOW THAT THESE COULD HAPPEN EARLIER. WHEN THESE THINGS DO HAPPEN, AGAIN, I THINK A VERY HONEST AND FRANK COMMUNICATION WITH THE PATIENT COMMUNITIES SURROUNDING WHAT DO WE KNOW NOW, WHAT IS THE NEW INFORMATION THAT HAS BEEN GAINED OVER THE LAST TWO YEARS, THREE YEARS, FOUR YEARS ABOUT THESE NEW ADVERSE EVENTS THAT WE HAVE IDENTIFIED? I THINK THAT NEEDS TO BE COMMUNICATED IN A PROACTIVE MANNER RATHER THAN AS A REACTIVE MANNER IN WHICH, OH, THIS HAPPENED. NOW WE HAVE TO SHUT THE TRIAL DOWN SO THERE WILL BE A PRESS RELEASE.

CO-CHAIRMAN FISHER: JEFF, I SEE YOUR

HAND.

CO-CHAIRMAN KAHN: THANKS. SORRY. MY HEADPHONE STOPPED WORKING. HOPEFULLY YOU CAN HEAR ME. I'M JUST TALKING THROUGH MY COMPUTER.

THE OTHER THING I WANTED TO ASK YOU, AKSHAY, WAS YOUR VERY GOOD POINT, I THINK, ABOUT CURE AND HOW PEOPLE UNDERSTAND THE TERM. AND THERAPEUTIC MISCONCEPTION HAS LONG BEEN A PROBLEM IN RESEARCH PARTICIPATION, AS I THINK WE ALL KNOW, I THINK MADE MORE COMPLICATED BY WHAT APPEAR TO BE KIND OF ONE AND DONE KINDS OF POTENTIAL THERAPIES.

AND SO I THINK AS WE EVEN MOVE THROUGH CLINICAL TRIALS AND INTO EVENTUAL APPROVALS, THINGS THAT SOUND LIKE ONE AND DONE ARE REALLY NOT, BUT THERE'S ONGOING NEED FOR TESTING AND MAYBE TREATMENT AND FOLLOW-UP AND ALL SORTS OF THINGS THAT MAKE IT MUCH LESS LIKE YOU'VE HAD ONE TREATMENT AND WE NEVER SEE UP AGAIN IN THE CLINIC. IT'S NOT THE WAY IT WILL WORK PROBABLY EVER.

AND SO I THINK PART OF THE TAKEAWAY HERE, AND THIS IS AGAIN A COMMENT, BUT I'D LOVE YOUR THOUGHTS ABOUT IT, IS THAT JUST IT WILL REQUIRE REALLY CAREFUL DISCLOSURES AND PROCESSES OF CONSENT AND UNDERSTANDING SO PEOPLE REALLY UNDERSTAND WHAT IT IS THEY'RE PARTICIPATING IN IN CLINICAL RESEARCH

AND THEN EVENTUALLY EVEN AS RECIPIENTS OF APPROVED THERAPIES. I THINK IT'S JUST KIND OF A NEW PHASE THAT WE'RE GOING TO HAVE TO FIGURE OUT HOW TO DEAL WITH.

DR. SHARMA: I COMPLETELY AGREE WITH YOU. THAT'S WHAT I WAS GETTING TO TOWARDS THE END OF MY TALK WHEN I SAID THAT A CURE WILL NEED TO BE DEFINED FOR EVERY PATIENT INDIVIDUALLY BECAUSE IT MAY MEAN DIFFERENT THINGS TO DIFFERENT PEOPLE. TO SOME PATIENTS IT MIGHT MEAN THAT THEY DON'T HAVE TO TAKE BLOOD TRANSFUSIONS ANYMORE. OR FOR SOME OTHER PATIENTS, IT MIGHT MEAN THAT THEY DON'T HAVE TO BE COMING TO HOSPITAL AS OFTEN. BUT LIKE DR. WAGNER WAS SAYING, WE HAVE NEVER ACTUALLY STUDIED THESE ENDPOINTS. WHAT HAPPENS TO PAIN? LIKE I SHOWED YOU, THERE WAS A PATIENT OF MINE WHO GOT GENE THERAPY, BUT HE'S STILL OPIOID DEPENDENT BECAUSE OF THE CHRONIC PAIN THAT HE HAS. NOW, THE GOOD THING IS THAT HE DOESN'T HAVE ANY ACUTE PAIN CRISES ANYMORE.

SO IN SOME WAYS, I WOULD SAY THAT HE IS IMPROVED. WOULD I CALL THAT A CURE? I PROBABLY WOULDN'T, BUT SOME OTHERS MIGHT AND THAT'S OKAY. SO THERE NEEDS TO BE THAT INDIVIDUALIZATION OF WHAT A CURE MEANS FOR EACH PATIENT.

CO-CHAIRMAN FISHER: SO I REALLY APPRECIATE THE TALK, THE TRANSPARENCY, AND YOUR SURFACING THESE ISSUES. WE HAVE LOTS OF EXAMPLES WHERE THE MEDIA IS JUST NOT OUR FRIEND WHEN IT COMES TO TALKING ABOUT WHAT'S HAPPENING IN THE THERAPY DEVELOPMENT SPACE. I'M SURE WE ALL GET E-MAILS FROM PATIENTS FREQUENTLY WHERE THEY'VE SEEN SOMETHING OR THEY'VE HEARD ABOUT IT. IS THIS -- WHAT DO I THINK? AND MAYBE WE NEED TO GET OURSELVES INVITED TO THE NEXT ETHICS AND MEDIA CONFERENCE ONCE WE HAVE A CLEAR PICTURE OURSELVES ABOUT WHAT WE MIGHT WANT TO SAY TO THE MEDIA ABOUT HOW THEY REPORT THIS.

AND PART OF WHAT'S DRIVING THAT IS THE MEDIA'S NEED FOR A GOOD STORY. AND THERE'S THIS VERY UNHEALTHY RELATIONSHIP, AND I'M NOT SAYING THAT THIS EXISTS WITHIN THE EXAMPLES YOU GAVE, BUT I THINK THERE ARE OTHER EXAMPLES WHERE IT EXISTS WHERE THE COMPANY THAT'S MOVING THESE TRIALS FORWARD HAS A FINANCIAL CONFLICT OF INTEREST. THEY'RE TRYING TO PUMP UP THEIR STOCK SHARES BY DISTORTING THE GOOD NEWS. AND SO WE HAVE THESE SORT OF PERFECT PARTNERS. THE COMPANIES WANT A WILLING PARTNER TO SHARE AN EXAGGERATED STORY ABOUT HOW GOOD THE NEWS IS, AND WE HAVE A PARTNER WHO NEEDS A GOOD STORY THAT EXAGGERATES REALITY. AND SO THERE'S A PROBLEM

INHERENT IN THE FINANCIAL CONFLICT OF INTEREST THAT EXISTS IN TRYING TO RAISE THE MONEY NECESSARY TO MOVE THESE THERAPIES FORWARD.

AND I'M ALWAYS VERY CAREFUL IN LOOKING AT PARTICULARLY THE LATE STAGE CLINICAL TRIALS THAT CIRM FUNDS FOR COMPANIES JUST BECAUSE OF THAT ISSUE. AND I THINK THE WHOLE CONVERSATION AROUND CURE DOES NEED TO EVOLVE, TO BE MORE NUANCED. IN NEURODEGENERATIVE DISEASES, I DON'T THINK ANYBODY IS REALLY TALKING ABOUT GETTING RID OF ALZHEIMER'S OR RESTORING A PERSON BACK TO THEIR PRESYMPTOMATIC STATE OR PARKINSON'S OR ALS OR ANY OF THEM EXCEPT MAYBE SMA AND THE EXPERIENCE THERE.

I THINK BY AND LARGE THE PHYSICIANS RUNNING THE TRIALS ARE MAYBE MORE CAUTIOUS ABOUT THAT WITH PATIENTS AND MORE UPFRONT ABOUT THAT WITH PATIENTS THAN THE SPONSORS OF THE TRIAL MIGHT BE. SO THERE'S A TENSION THERE ALSO AS THE PATIENT HAS TO RECONCILE THE HYPE.

BY THE WAY, I JUST LEARNED TODAY THAT HYPE IS -- THE ROOT WORD OF HYPE IS HYPERBOLIC. I NEVER MADE THAT CONNECTION BEFORE. SO THANK YOU ALL FOR THAT.

THE PATIENTS AND THE CLINICIANS ARE IN A POSITION TO SORT OF TAMP DOWN THE ENTHUSIASM THAT

MIGHT BE COMING FROM THE COMPANY AND THE MEDIA THAT'S ACTUALLY SPONSORING THE TRIAL. SO COMPLICATED SPACE. I JUST WANTED TO THROW THAT OTHER DYNAMIC OUT THERE, THAT THE EXAGGERATION IS NOT JUST DRIVEN BY THE MEDIA NEEDING A GOOD STORY. IN SOME CASES IT'S ALSO THE COMPANIES NEEDING TO KEEP THEIR STOCK PRICE AFLOAT AND ATTRACT NEW INVESTORS.

DR. WAGNER: CAN I RESPOND TO THAT THOUGH? I HAVE TO SAY THAT THAT IS A COMMON BELIEF, BUT THAT'S REALLY NOT BEEN MY EXPERIENCE. I THINK THAT THE BIOTECH COMPANIES IN PARTICULAR ARE HYPERSENSITIVE AS TO WHAT CAN BE SAID. IN FACT, ACTUALLY EVEN WITH THIS TRIAL WITH BLUEBIRD OR OTHER TRIALS THAT YOU'RE INVOLVED IN, CAN ATTEST TO, THE COMPANIES ARE ACTUALLY MONITORING WHAT COMES OUT OF OUR MOUTHS BECAUSE THEY WANT TO MAKE SURE THAT IT'S NOT, NO. 1, THAT INFORMATION THAT'S NOT YET DISCLOSED BY THE COMPANY. THEY DON'T WANT THAT TO COME OUT. BUT IN ADDITION, THEY ALSO WANT TO MAKE SURE THAT THERE IS NO OVERINTERPRETATION OF THE DATA.

SO I AGREE WITH YOU THAT THERE IS A RISK, AND I CAN'T SAY CERTAINLY, I'M SURE THERE'S MANY EXAMPLES WHERE THAT IS TRUE WHERE THE COMPANY MAY

SAY SOMETHING DIFFERENTLY. AT LEAST MAYBE IN MORE RECENT YEARS, I FEEL EVERYONE IS MUCH MORE CAREFUL.

BUT IN ADDITION, I THINK THAT, IN TERMS OF HOW WE DEAL WITH MEDIA, IT IS MORE DIFFICULT BECAUSE I'VE HAD THE EXPERIENCE WHERE I TALK ABOUT A RESULT AND THEY COME BACK AND THEY WILL SAY, "I CAN'T READ WHAT THEY'VE WRITTEN IN ADVANCE." SO THEY MAY HAVE TALKED TO ME, BUT YET THEN THEY WRITE THEIR STORY, AND IT MAY NOT BE THE SAME STORY THAT I PRESENTED. BUT MORE AND MORE FREQUENTLY, I WILL DEMAND TO READ IT UPFRONT OR I DON'T GIVE THE INTERVIEW.

ON THE OTHER HAND, THAT'S THE PART THAT IS HARD WITH WRITING STORIES ABOUT THE WORK THAT WE DO. IN ANY CASE, I STILL THINK IT ALL COMES DOWN TO THE CONSENT PROCESS AND BEING ABLE TO REALLY BREAK IT DOWN INTO ITS COMPONENTS. BOY, THIS IS REALLY A STRUGGLE BECAUSE IT'S COMPLICATED IN WHAT WE ARE DOING AND BREAKING IT DOWN INTO WHAT ARE WE LOOKING TO ACHIEVE RIGHT NOW VERSUS THE FUTURE.

ONE LAST COMMENT. IF I HAD TO SAY HOW DO WE LIVE UP TO CIRM'S GOAL OF BEING ABLE TO DEVELOP PRODUCTS THAT ARE GOING TO BE READILY AVAILABLE TO THE PUBLIC IN SOME WAY, I WOULD SAY TO YOU THAT, IF WE WANT TO DO THAT AND ACHIEVE THIS IN AFRICA, FOR EXAMPLE, THEN WHAT WE ARE DOING RIGHT NOW IS NOT THE

RIGHT WAY. WHAT WE'D BE DOING IS DEVELOPING IN VIVO GENE THERAPY WHERE YOU CAN INJECT THE MATERIAL AND THEN WALK AWAY. BUT COLLECTING HEMATOPOIETIC STEM CELLS, GIVING BUSULFAN IN ADVANCE, AND TRANSFUSION IS REQUIRED, THIS IS NOT WHAT'S GOING TO MAKE THIS READILY AVAILABLE. BUT WHAT IT IS IT'S A STEP IN THE LONG-TERM PIPELINE OF PLANS. MAYBE WE NEED TO PRESENT THAT TOO, AT LEAST IN TERMS OF THE GWG. THIS IS STEP ONE IN A LONGER PHASE STUDY, AND THE FDA LIKES THAT AS WELL. JUST A COMMENT.

CO-CHAIRMAN KAHN: LET ME INTERJECT HERE JUST BECAUSE I WANT TO CHECK TIME. GEOFF LOMAX, WHERE ARE WE? HOW MANY MORE COMMENTS CAN WE TAKE?

DR. LOMAX: TIME IS NOT A CONSIDERATION, BUT WE DO HAVE ONE OTHER SORT OF SHORT SET OF COMMENTS FROM ANOTHER CLINICIAN THAT WE THOUGHT WOULD COMPLEMENT THIS, DR. FARMER. SO I'D LIKE TO -- MAYBE WE COULD TAKE ONE OR TWO MORE COMMENTS AND THEN INVITE HER TO MAKE SOME COMMENTS JUST TO KIND OF GIVE A CONTRAST JUST SO WE A LITTLE MORE DIVERSITY IN TERMS OF THE CLINICAL PROFILES WE'RE LOOKING AT HERE. SO IF THAT'S OKAY, COULD WE TAKE THE LAST TWO COMMENTS AND THEN SEE IF DR. FARMER WOULD LIKE TO COMMENT?

CO-CHAIRMAN KAHN: THAT SOUNDS GOOD.

OKAY. CHRIS AND THEN MARIA. CHRIS.

DR. SAHA: SURE. I THINK, AKSHAY, THAT WAS A REALLY NICE PRESENTATION. I ALMOST ENTIRELY AGREE WITH A LOT OF THE CRITIQUES AND COMMENTARY HERE. I WAS JUST WONDERING ALSO OF MAKING A COMMENT HERE, THAT WE MIGHT BE ASKING TOO MUCH OUT OF CONSENT IN THAT THE KIND OF OTHER TOOLS THAT ARE AVAILABLE HERE ARE RICH AND INTERESTING. AND PERHAPS COLLECTIVELY WE CAN CREATIVELY THINK OF THAT TOOL SET AS BEING PART OF AN INFRASTRUCTURE THAT COMPLEMENTS AND BUILDS UPON THE ALPHA CLINICS.

AND SO THERE'S MANY REASONS FOR WHY ALMOST EVERYONE IMMEDIATELY GOES TO CONSENT, BUT COULDN'T WE THINK ABOUT DEFINING CURE IN THE INDIVIDUAL FASHION FOR ANY TYPE OF PRODUCT THAT COMES OUT OF AN ALPHA CLINIC? THAT DOESN'T HAVE TO BE LEGALLY BINDING, BUT IT COULD BE A BEST PRACTICE OR STANDARD.

AND I JUST THINK HOW I SEE THIS TYPE OF CONCERNS AS BEING AN EXTRA SET OF INFRASTRUCTURE, MAYBE NOT PHYSICAL INFRASTRUCTURE, BUT ETHICAL INFRASTRUCTURE THAT BUILDS UPON THE ALREADY INTERESTING AND CONSIDERABLE INVESTMENT THAT CIRM HAS MADE ON THE ALPHA CLINICS.

DR. SHARMA: I COMPLETELY AGREE WITH YOU,

CHRIS. AND THAT'S WHAT I SORT OF ENVISIONED WHEN I SAY INFORMED CONSENT 2.0 IS THAT THERE WILL BE THIS HUGE INFRASTRUCTURE, WHETHER THAT IS IN THE FORM OF WEBSITES, APPS, BOOKS, AUDIOVISUAL AIDS THAT PATIENTS CAN NAVIGATE THROUGH AT THEIR OWN LEISURE, WHICH WILL BE SUPPORTED BY PATIENTS, SCIENTISTS, CLINICIANS LIKE OURSELVES AND PROVIDE A MORE BALANCED APPROACH TO THE PATIENTS ABOUT WHAT THEY REALLY NEED. AND THAT WILL SUPPLEMENT THE INFORMED CONSENT, THE PAPER-BASED INFORMED CONSENT THAT WE HAVE RIGHT NOW. SO COMPLETELY AGREE WITH WHAT YOU JUST SAID.

DR. SAHA: JUST ONE QUICK COMMENT ON THAT. I KNOW ASPCT HAS ALREADY STARTED ON THIS IN SOME WAY. I'M JUST CURIOUS, I GUESS, TO THE ENTIRE GROUP WHAT WOULD BE DIFFERENT AND SPECIAL, SPECIFIC TO CALIFORNIA, FOR INSTANCE, OR AUGMENTED ON TOP OF WHAT THEY'RE DOING AT THE NATIONAL LEVEL. THAT'S ALL I HAD. THANKS.

CO-CHAIRMAN KAHN: IT'S A QUESTION WE SHOULD CONTINUE TO TALK ABOUT. THANK YOU FOR ASKING IT, CHRIS. AND HOW CAN CALIFORNIA CONTRIBUTE AND CIRM CONTRIBUTE, I GUESS, MAY BE ONE WAY TO PUT IT.

DR. MILLAN, YOU GET THE LAST WORD, I THINK, AT THIS POINT.

DR. MILLAN: THANK YOU SO MUCH. AND REALLY APPRECIATE THIS CONVERSATION BECAUSE THAT "C" WORD, THAT CURE WORD WAS SOMETHING THAT WE GRAPPLED WITH YEARS AGO WHEN WE HAD THE INITIAL DATA FROM THE ADA-SCID TRIAL. WE ARE BALANCING HOW DO WE INFORM THE PUBLIC IN TERMS OF WHAT THE PROGRESS HAS BEEN WITH THE DOLLARS THAT THEY'VE INVESTED INTO THIS RESEARCH, AND IS IT REALLY GOING ANYWHERE. WE'RE SHORT OF HAVING ANY APPROVED PRODUCTS. IT'S REALLY DIFFICULT TO ARTICULATE SCIENTIFIC PROGRESS.

SO WE ARE VERY WELCOMING OF ANY TYPE OF DIRECTION THAT WE CAN TAKE SO THAT WE HAVE A BETTER ARTICULATED RATIONALE FOR WHY IN CERTAIN CASES YOU WOULD USE THAT WORD. IN MOST CASES OUR COMMUNICATIONS TEAM, WE WORK VERY DILIGENTLY TO MAKE SURE THAT WE REPRESENT WHEN THERE'S PROMISING DATA, WHAT DOES THAT PROMISING DATA MEAN. SO THEY MAY BE -- AND TRYING TO PUT IT IN A DIGESTIBLE FORMAT SO THAT THE GENERAL PUBLIC UNDERSTANDS WHAT THE INTERIM PROGRESS IS.

SO THAT'S ONE THING BECAUSE WE ALSO STRUGGLE WITH MAKING SURE THAT WE ARE RESPONSIBLE FOR REPORTING OUT TO THE PUBLIC. BUT ANOTHER TREND THAT'S HAPPENING IS MORE AND MORE EARLY RESULTS WITH THE FIRST PATIENT DOSE OR THE FIRST COUPLE OF

PATIENTS DOSE ARE BEING PUBLICIZED, AND THEY'RE ACTUALLY BEING PUBLISHED. AND PUBLISHERS THEMSELVES IN THE HIGH IMPACT SCIENTIFIC JOURNALS DO BELIEVE IT'S IMPORTANT BECAUSE NOW THEY'RE EMBRACING THE TRANSLATIONAL IMPACT OF THE SCIENCE AND UNDERSTANDING KIND OF THAT CONTINUUM.

SO WE ARE IN A VERY INTERESTING AND IMPORTANT PHASE RIGHT NOW. AND DEFINING IT AS WAS PROPOSED, USING MECHANISMS AS CHRIS HAD ALLUDED TO IN TERMS OF MAKING SURE THAT WHEN WE HAVE OPPORTUNITIES WITHIN OUR GRANTS OR WITHIN OUR ALPHA CLINICS OR INSTITUTIONS THAT WE FUND TO GET SOME ALIGNMENT IN TERMS OF USE OF TERMS OR APPROACHES TO HOW THE PATIENTS ARE INFORMED IN TERMS OF WHAT THE TRUE VALUE PROPOSITION IS FOR THEM ENTERING A TRIAL. I THINK THAT'S REALLY IMPORTANT. SO THANK YOU FOR TODAY'S DISCUSSION.

CO-CHAIRMAN KAHN: FRED, I THINK AS CO-CHAIR YOU GET TO HAVE THE LAST, LAST WORD.

CO-CHAIRMAN FISHER: WELL, WE CAN PUT A PIN IN THIS. I THINK THIS GROUP CAN BE HELPFUL TO CIRM ITSELF BECAUSE CIRM HAS HAD CHALLENGES AROUND THE WORD "CURE." CIRM JUSTIFIED ITS EXISTENCE ON THE DISCOVERY OF CURES. AND SO CIRM IN ITS OWN WAY MIGHT HAVE CONTRIBUTED OR AS PART OF THE SPACE IS AS

GUILTY AS ANYONE ELSE FOR SORT OF HYPING THE CURES THAT WILL COME OUT OF THIS $5.5 BILLION INITIATIVE.

AND SO AS WE HAVE THIS CONVERSATION, IN ADDITION TO SORT OF LOOKING OUTWARD INTO THE SPACE, THIS GROUP CAN BE HELPFUL AT HELPING US IN LOOK INWARD IN TERMS OF HOW WE EVOLVE OUR OWN NARRATIVE AROUND THESE THINGS IN A WAY THAT, NO. 1, MAINTAINS THE PUBLIC SUPPORT FOR WHAT WE ARE DOING, BUT DOES IT IN AN HONEST AND TRANSPARENT WAY.

DR. LOMAX: I WAS JUST LOOKING. DO WE HAVE DR. FARMER ON THE ZOOM? I'M JUST CHECKING. I'M JUST WONDERING IF SHE'S BEEN ABLE TO JOIN. IS THERE ANYONE DIALING IN ON THE COMMENT SIDE? OTHERWISE WE CAN JUST CONTINUE WITH THE CURRENT DISCUSSION.

DR. WAGNER: ONE EXAMPLE THAT JUST CAME OUT THIS WEEK ON THIS PARTICULAR TOPIC OF SICKLE CELL DISEASE AND THALASSEMIA WAS THE JASPER ANNOUNCEMENT. IT CAME ON JANUARY 3D. I THINK, FRED, IT GETS TO YOUR POINT WHICH YOU WERE MAKING EARLIER, THAT EVERYTHING WAS WRITTEN ACCURATELY, BUT YOU COULD IMAGINE HOW THE PUBLIC WOULD VIEW IT DIFFERENTLY. SO THIS IS WITH AN ANTIBODY TO IMPROVE CONDITIONING OR TO MAKE CONDITIONING SAFER. AND IN THE CONTEXT OF HEMOGLOBINOPATHY, THERE WERE THREE

PATIENTS THAT RECEIVED THE JASPER ANTI-C-KIT PRODUCT WHICH WAS DIRECTED AT ERADICATING RESIDUAL HOST CELLS. AND THAT'S ONE WAY OF GETTING RID OF THE ABERRANT CELL POPULATION WITHOUT GIVING ADDITIONAL CHEMOTHERAPY.

THE WAY THE PRESS RELEASE IS WRITTEN, IT DOES MAKE IT SOUND LIKE THAT THEY DEMONSTRATED SOMETHING -- WELL, THE TITLE IS "JASPER'S THERAPEUTIC ANNOUNCES POSITIVE CLINICAL DATA FROM PHASE 1-2 TRIAL OF BRIQUILIMAB AS A CONDITIONING TREATMENT FOR SICKLE CELL DISEASE AND THALASSEMIA." AND THEN THE CEO OF JASPER SAYS, "WELL, STEM CELL INFUSIONS WOULD HELP THE DONOR CELLS OR GENE-CORRECTED CELLS AS A POTENTIALLY CURATIVE OPTION FOR SICKLE CELL AND BETA THALASSEMIA. THEY ARE BOTH LIMITED BY THE TOXICITY OF THE CURRENT CONDITIONING REGIMENS USING BUSULFAN OR MELPHALAN, WHICH ARE OFTEN CITED AS THE MOST CONCERNING SAFETY RISKS BY TRANSPLANT PATIENTS AND PHYSICIANS. WITH THE ANTIBODY, WE HOPE TO OFFER A HIGHLY TARGETED CONDITIONING TO DIRECTLY ADDRESS CONDITIONING TOXICITY, A BARRIER LIMITING THE ABILITY OF PATIENTS TO ACCESS CURATIVE HEMATOPOIETIC STEM CELL THERAPIES."

NOW, THE WAY THE TRIAL WAS DESIGNED WAS

REALLY ADDING THIS ANTIBODY TO ANOTHER NON-MYELOABLATIVE CONDITIONING AGENT. IT'S ONLY IN SEVERAL PATIENTS. I DON'T KNOW HOW MANY PATIENTS HAD SICKLE CELL VERSUS BETA THALASSEMIA. BUT YOU CAN IMAGINE HOW THE PATIENTS WITH SICKLE CELL AND BETA THALASSEMIA SEE, OH, I CAN GET RID OF BUSULFAN, WHICH IS NOT EXACTLY WHAT THEY SHOWED. IS THE RESULT INTERESTING? YES, IT'S VERY INTERESTING BECAUSE THEY GOT RID OF MIXED CHIMERISM AT LEAST IN A COUPLE OF PATIENTS, BUT THAT'S A NUANCE THAT THE PUBLIC WOULD NEVER CATCH.

SO HOW WE PRESENT THAT BEST, WE'VE ALREADY TALKED ABOUT THAT, BUT IT'S JUST APPROPRIATE FOR TODAY'S DISCUSSION. THIS JUST OCCURRED A FEW DAYS AGO.

DR. SHARMA: I WOULD ALSO ADD THAT SOME OF THE ENDPOINTS, YOU MIGHT HAVE NOTICED, DR. WAGNER, THEY TALKED ABOUT A TWO-MONTH CHIMERISM RESULT OVER THERE. IF WE DELVE DEEP INTO THE DATA, TWO-MONTH CHIMERISM DOESN'T REALLY MEAN MUCH. I MEAN YOU HAVE TO LOOK AT LONG TERM. AND SO SAYING THAT SOMETHING WAS A HUNDRED PERCENT AT TWO MONTHS, IT LOOKS GOOD, BUT THE REAL PRIZE IS AT ONE YEAR AND TWO YEAR. AND SO, AGAIN, MASSAGING THE DATA A LITTLE BIT, YOU MIGHT BE ABLE TO PUBLICIZE, SIMILAR TO WHAT MARIA

WAS SAYING EARLIER, WHO CONTROLS THE FLOW OF THIS INFORMATION TO THE PUBLIC? EVERYBODY INVOLVED IN THESE, EITHER THE MEDIA OR THE COMPANIES, THEY SORT OF ALL WANT TO PROJECT THE POSITIVE INFORMATION.

AND LIKE YOU MENTIONED EARLIER, OF COURSE, AS CLINICIANS AND SCIENTISTS, WE WANT TO BE AS ACCURATE AS POSSIBLE, AND THERE WAS NOTHING WRONG IN THAT PRESS RELEASE. IT WAS ALL ACCURATE, BUT STILL IT WAS HYPERBOLIC, AND IT CAN MISLEAD DEFINITELY PATIENTS, BUT ALSO POTENTIALLY OTHER CLINICIANS WHO MAY NOT BE AS DISCERNING OF THESE DATA.

DR. LOMAX: DR. GOLDSTEIN, DO YOU HAVE A COMMENT?

DR. GOLDSTEIN: YEAH. I DO. WHILE IT'S ALL WELL AND GOOD TO BEAT UP ON OUR CLINICAL COLLEAGUES, THEY CERTAINLY DO WRITE PRESS RELEASES THAT ARE SOMETIMES SUSPECT. I DON'T THINK WE'RE FREE OF THAT IN THE ACADEMIC SECTOR EITHER. YOUNG SCIENTISTS AND CLINICIANS ARE TRYING TO GET TENURE. MORE EXPERIENCED SCIENTISTS ARE TRYING TO GET GRANTS OR ELECTED TO ACADEMIES OF ONE SORT OR ANOTHER. I DON'T THINK YOU'RE EVER GOING TO COMPLETELY ERADICATE THE PROBLEM OF BIAS.

I THINK A BETTER WAY TO TACKLE THE PROBLEM IS TO ASK HOW DO YOU BEST GET GOOD INFORMATION OUT

TO PATIENTS. AND I THINK AT THE MOMENT WE DON'T HAVE THAT MANY AVENUES. PATIENT ADVOCACY GROUPS ARE ONE REALLY IMPORTANT WAY OF DOING IT. REPUTABLE SOURCES, SUCH AS CIRM, WHICH I HOPE IS A TRUSTED SOURCE, ALTHOUGH THE PROBLEM WITH THE LANGUAGE OF CURES WAS JUST POINTED OUT A FEW MINUTES AGO. IT'S SOMETHING THAT WE ARE ALL GOING TO HAVE TO COLLECTIVELY WORK ON OVER TIME BY INFLUENCING OURSELVES AND INFLUENCING OUR COLLEAGUES.

DR. LOMAX: MAYBE I CAN JUST ADD. I WON'T BOTHER PULLING UP THE SLIDE. WE HAD A -- ACTUALLY TO SORT OF TEE UP THIS CONVERSATION, WE DID HAVE A SET OF QUESTIONS. AND I JUST WANTED TO PUT THEM BACK OUT THERE TO MAKE SURE WE'VE COVERED THAT GROUND OR TO PUT THEM OUT THERE FOR THE FIRST TIME.

TWO OF THE QUESTIONS IN PARTICULAR THAT WE HAD FOR THIS GROUP, AND THEY WERE ALREADY ALLUDED TO, I THINK THE ASGCT EFFORTS. ARE THERE EXISTING EITHER RESEARCH INITIATIVES THAT COULD BENEFIT FROM ADDITIONAL -- INCREASING THE DENOMINATOR, IF YOU WILL, IN CALIFORNIA BECAUSE WE HAVE PATIENTS OR DE NOVO ETHICS POLICY RESEARCH NEEDS BECAUSE WE HAVE THE OPPORTUNITY TO SUPPORT RESEARCH. ARE THERE THINGS WE CAN DO AT MORE OF AN EMPIRICAL LEVEL TO EITHER SUPPORT EXISTING INITIATIVES OR TO ADDRESS

QUESTIONS THAT ARE BEING DISCUSSED AMONGST -- I KNOW THERE'S A LOT OF -- I KNOW THIS CONVERSATION IS GOING ON INTERNATIONALLY.

SO THAT WAS A COUPLE OF THE QUESTIONS WE HAD FOR YOU. I DON'T KNOW IF WE'VE EXHAUSTED THOSE COMMENTS, OR OF THERE'S COMMENT THAT COULD BE ADDED.

CO-CHAIRMAN KAHN: AKSHAY, GO AHEAD.

DR. SHARMA: SO I GUESS I CAN ANSWER THAT. SO NIH STARTED -- NHGRI ACTUALLY STARTED THIS ENDEAVOR CALLED "DEMOCRATIZING SCD" SOMETIME LAST YEAR. THEY DID SOMETHING VERY SIMILAR. THEY GOT TOGETHER A BUNCH OF CLINICIANS, PATIENTS, ADVOCATES, PHARMACEUTICAL INDUSTRY REPRESENTATIVES, AND THEY ASKED THE QUESTION: WHAT DO YOU WANT TO HAVE IN AN EDUCATIONAL INFORMED CONSENT DOCUMENT AROUND SICKLE CELL DISEASE? AND SO BY DOING THAT, THEY'RE ALREADY SORT OF WORKING ON DEVELOPING PATIENT EDUCATION MATERIALS, WHICH IS ONE SUCH EXERCISE.

OUR GROUP, LED BY MYSELF AND DR. LIZA JOHNSON HERE, WE HAVE BEEN WORKING ON SOMETHING SIMILAR IN DESIGNING CARTOONS AND AUDIOVISUAL AIDS WHICH WILL HELP PATIENTS NAVIGATE THROUGH THIS WHOLE PATHWAY AS WELL. AND SO THERE ARE MULTIPLE DIFFERENT EFFORTS WHICH I THINK, JEFF, AS WAS ALLUDED TO IN THE DISCUSSION IN THE MORNING, I THINK

YOU HAD SAID THAT ONE PLUS ONE EQUALS THREE. I THINK THAT IS DEFINITELY WHAT WE SHOULD ENVISION AND TRY TO DO OVER HERE BY CONNECTING DIFFERENT STAKEHOLDERS AND DIFFERENT GROUPS DEVELOPING THESE RESOURCES, POTENTIALLY PARTNERING WITH ALL THE ALPHA CLINICS THAT YOU HAVE, SO THAT YOU CAN INVOLVE BOTH PATIENTS AS WELL AS CLINICIANS AND OTHERS FROM ALL THESE AVENUES, THAT YOU CAN DEVELOP MATERIAL WHICH IS GLOBAL IN ORIGIN AND APPEAL AND WHICH HAS A MUCH DIVERSE VIEWPOINT AND INFORMATION THAT THEN IS APPLICABLE TO MORE THAN JUST A FEW HUNDRED OR FEW THOUSAND PATIENTS. DOES THAT MAKE SENSE?

CO-CHAIRMAN KAHN: YEAH. IT DEFINITELY MAKES SENSE. THIS IS THE KIND OF BRAINSTORMING I THINK GEOFF IS ASKING US TO DO.

MY ANSWER TO YOUR QUESTION, GEOFF, IS THAT I'M NOT FEELING LIKE I KNOW A HUNDRED PERCENT ABOUT WHAT'S HAPPENING ELSEWHERE. SO I DON'T KNOW HOW WE MIGHT GO ABOUT TRYING TO COLLECT INFORMATION ABOUT THAT. HOW CAN WE COLLABORATE WITH THINGS? WE HEARD ABOUT ASCGT WHICH I THINK WE ALL KNOW, AND AKSHAY JUST MENTIONED SOME NHGRI INITIATIVES. IT WOULD BE GOOD FOR US TO TRY FIGURE OUT IF WE CAN GET A LIST OR A COLLECTION OF WHAT'S HAPPENING ELSEWHERE THAT WE MIGHT THEN BUILD ON AND/OR COLLABORATE WITH.

GEOFF, DID WE LOSE YOU?

DR. MILLAN: WE LOST GEOFF.

CO-CHAIRMAN KHAN: LOOKS LIKE IT.

DR. MILLAN: I THINK THAT THIS IS A REALLY GOOD DISCUSSION. WE SHOULD -- THE TEAM WILL FOLLOW UP WITH CHRIS IF YOU CAN CONNECT US AT ASCGT AND AKSHAY AT THE NHGRI SO WE CAN HAVE A LOOK AT WHAT'S ALREADY IN PLACE AND EVALUATE THAT. GEOFF, I WAS FILLING IN. THERE YOU ARE.

DR. LOMAX: I'M SORRY. THERE WAS A MINOR DISASTER HERE, BUT I'M BACK.

DR. MILLAN: BUT I DID COMMIT US TO MAKING SURE THAT WE FOLLOWED UP WITH THE INITIATIVES THAT ARE ALREADY ONGOING AT ASGCT AND AT NHGRI AND IDENTIFY OTHER INITIATIVES, AS PER DR. KAHN'S RECOMMENDATION, TO REALLY DO SOME INTELLIGENCE GATHERING AND THEN GO FROM THERE REGARDING THIS MOST RECENT TOPIC.

CO-CHAIRMAN KAHN: I DON'T KNOW IF YOU HEARD THAT PART, GEOFF. JUST TRYING TO FIGURE OUT A BETTER SENSE OF THE WATERFRONT.

DR. LOMAX: I GOT THAT. JUST ONE OTHER THING TO NOTE. I THINK WE DID WANT TO OFFER THE OPPORTUNITY IF THERE ARE COMMENTS. I THINK SOME OF THE OTHER STAKEHOLDERS MAYBE MAY HAVE PUBLIC COMMENT

OR STAKEHOLDER COMMENTS. JUST TO GIVE FOLKS A HEADS-UP, THAT WE ARE HAPPY TO TAKE COMMENTS DURING THIS SEGMENT AS WELL. I KNOW SOMETIMES IT TAKES PEOPLE A FEW MINUTES TO NAVIGATE THE PUBLIC COMMENT SYSTEM. SO IF YOU WOULD LIKE TO MAKE A COMMENT ON THIS SEGMENT, PLEASE FEEL FREE TO DO SO AND WE'LL ENTERTAIN THOSE AS WELL. PAUSE HERE. IF FOLKS SORT OF MONITORING THE DIAL-IN SITE, DO WE HAVE ANY COMMENTS? MARIVEL, DO YOU KNOW?

MS. DE LA TORRE: I HAVEN'T SEEN ANY COMMENTS AS OF YET, BUT I'LL LET YOU KNOW.

MS. DEQUINA-VILLABLANCA: NEITHER HAVE I.

DR. LOMAX: OKAY. LIKE I SAY, THAT'S AN OPEN OFFER. ARE THERE OTHER COMMENTS OR SUGGESTIONS FOR THIS SEGMENT? IF THAT'S THE CASE, WE CAN TAKE A SHORT BREAK. I THINK WE HAD A 15-MINUTE BREAK SCHEDULED FOR THE CONCLUSION OF THIS SEGMENT. THAT WOULD PUT US AT 1 O'CLOCK. SO WE COULD CONVENE AT 1 O'CLOCK AND JUST HAVE SOME WRAP-UP DISCUSSION. I THINK WE'LL AT THIS POINT PROBABLY BE FINISHED CERTAINLY BEFORE 2 O'CLOCK, PERHAPS 1:30 AT THIS TIME. SO IF THAT'S OKAY, WE CAN RECONVENE IN 15 MINUTES.

CO-CHAIRMAN KAHN: GREAT. THANK YOU.

(A RECESS WAS TAKEN.)

DR. LOMAX: WE'RE BACK AT THE TOP OF THE HOUR. QUESTION, ASSUMING NO ONE TRIED TO COME IN TO COMMENT; IS THAT CORRECT?

MS. DEQUINA-VILLABLANCA: YES.

DR. LOMAX: WE HAVE PUBLIC COMMENT SLATED FOR THE END OF THE MEETING AS WELL. SO FOLKS ARE AWARE.

SO ONE LAST PRESENTATION. THE SLIDES ARE COMING UP. AN OVERVIEW OF OUR POLICY FRAMEWORK THAT GUIDES OUR MEDICAL AND ETHICAL STANDARDS. THE END GAME REALLY IS TO CONSIDER -- IS TO CONSIDER IF THERE ARE THINGS WE NEED TO BE THINKING ABOUT LOOKING FORWARD. I MENTION THAT BECAUSE, AFTER SUCH A ROBUST DISCUSSION ABOUT THE CONSENT ISSUES, IT'S SOMETIMES A LITTLE TRICKY SEGUE TO GET BACK INTO REGULATIONS, BUT WE DO WANT TO JUST GET YOUR INPUT IN TERMS OF THINGS WE NEED TO BE THINKING ABOUT. SO I'LL TRY TO MOVE THROUGH THIS FAIRLY QUICKLY, AND WE'LL GET TO DISCUSSION. NEXT SLIDE.

LET'S GO TO THE NEXT SLIDE. WE COVERED THAT. AND ONE MORE PLEASE. SO WE'VE CIRCULATED A COUPLE OF TIMES AN OVERVIEW OF OUR MEDICAL AND ETHICAL STANDARDS. AND ALTHOUGH THIS DOCUMENT IS A BIT DATED, I THINK WE CAN STILL -- IT DOES A PRETTY NICE JOB OF LAYING OUT THE FACT THAT FUNDAMENTALLY

CIRM IS COMMITTED TO THE RESPONSIBLE OVERSIGHT OF RESEARCH AND THAT WE'VE DEVELOPED PARTICULAR POLICIES AND STANDARDS TO SUPPORT BEST-IN-CLASS RESEARCH. AND WE'VE DONE THAT IN A WAY THAT'S ALIGNED WITH FEDERAL POLICY TO A LARGE EXTENT BECAUSE THAT MAKES FOR EFFICIENCY AND EFFECTIVENESS. WE ARE NOT TRYING TO OVERBURDEN THE RESEARCH ENTERPRISE EITHER. SO NEXT SLIDE PLEASE.

SO FUNDAMENTALLY OUR POLICIES THAT WE HAVE DEVELOPED AND CONTINUE TO MODIFY AND MAINTAIN ARE REALLY A SET OF POLICIES THAT WERE DEVELOPED BY THE NATIONAL ACADEMIES THROUGH THEIR HUMAN EMBRYONIC STEM CELL RESEARCH GUIDELINES AND REALLY JUST TO FILL GAPS IN FEDERAL POLICY FOR WHICH THERE WAS CONSENSUS THERE NEEDED TO BE OVERSIGHT AND GUIDANCE TO THE RESEARCH COMMUNITY. SO, AGAIN, THOSE WERE ACTIVITIES THAT WOULD NOT BE COVERED UNDER FEDERAL POLICY AND, FOR THE MOST PART, INVOLVE EMBRYO RESEARCH, THE USE OF HUMAN EMBRYONIC STEM CELL LINES AND THEIR DERIVATION. FEDERAL POLICY NOW ALLOWS FOR BROADER USE OF THE STEM CELL LINES, BUT STILL PROHIBITS THEIR DERIVATION. SO THE POLICIES REMAIN RELEVANT. NEXT SLIDE PLEASE.

SO, AGAIN, THE SCOPE IS CIRM-FUNDED PROJECTS AND ACTIVITIES. SO THESE ARE POLICIES THAT

PERTAIN SPECIFICALLY TO OUR RESEARCH AWARDS. HOWEVER, CALIFORNIA DID ADOPT GUIDELINES IN 2006 THAT APPLY THE CIRM POLICIES TO RESEARCH GENERALLY IN THE STATE, BUT THEY ADOPTED THEM AS GUIDELINES. SO IT'S MORE OF A GUIDANCE OPPOSED TO THE POLICIES THAT CIRM PROMULGATES WHICH ARE TIED TO THE RESEARCH AWARDS. SO IN A SENSE WE HAVE A VERY ACTIVE SYSTEM FOR MONITORING AND ENSURING COMPLIANCE. NEXT SLIDE PLEASE.

SO JUST A FEW THINGS THAT I THINK ARE IMPORTANT THAT WE WOULD PUT IN THE CATEGORY OF RESTRICTIONS. PROPOSITION 71 INITIALLY AND PROP 14 REITERATED THAT HUMAN REPRODUCTIVE CLONING IS IN NO WAY ALLOWED USING CIRM FUNDING. AND IN ADDITION, THERE'S A LIMIT ON THE CULTURE OF HUMAN EMBRYOS. AND WHILE THE INTERNATIONAL CONSENSUS CURRENTLY IS AT 14 DAYS, UNDER OUR RULES IT'S ACTUALLY A 12-DAY LIMIT. SO SOMETHING TO BE AWARE OF.

AND THEN CONSISTENT WITH THE NATIONAL ACADEMIES GUIDELINES, THERE'S A SET OF RESTRICTIONS IN TERMS OF THE UTILIZATION OF HUMAN STEM CELLS, PARTICULARLY THAT THEY NOT BE INTRODUCED INTO PRIMATE EMBRYOS. THERE'S CURRENTLY A RESTRICTION ON BREEDING OF ANIMALS IN WHICH HUMAN PLURIPOTENT STEM CELLS HAVE BEEN INTRODUCED AND THE USE OF

GENETICALLY MODIFIED EMBRYOS FOR HUMAN REPRODUCTION, WHICH CURRENTLY IS THE CONSENSUS STANDARD, CONSENSUS INTERNATIONALLY, AND CONTINUES TO BE. THIS IS INVOLVING THE CRISPR TECHNOLOGIES. NEXT SLIDE PLEASE.

AND IN TERMS OF HOW THESE RULES, THE OPERATIONAL ASPECTS OF THESE RULES, WE CONTINUE TO REQUIRE THAT A COMMITTEE, THE EMBRYONIC STEM CELL RESEARCH OVERSIGHT COMMITTEE, REVIEW AND APPROVE PROTOCOLS INVOLVING EITHER THE USE OF HUMAN OOCYTES OR EMBRYOS. AND THIS WOULD -- IN ADDITION TO OOCYTE/EMBRYO RESEARCH, THE SAME REVIEW AND OVERSIGHT REQUIREMENT WOULD APPLY TO BLASTOCYST COMPLEMENTATION STUDIES OR THE INTRODUCTION OF NEURAL PROGENITORS INTO THE BRAINS OF NONHUMAN ANIMALS. SO BULLET 2, THERE'S A SET OF SORT OF HUMAN ANIMAL RESEARCH THAT IS ALSO SUBJECT TO REVIEW AND OVERSIGHT.

AND OUR REQUIREMENT -- OUR POLICIES ALSO INCLUDE REQUIREMENTS FOR RESEARCH INVOLVING HUMAN OOCYTES. THEY'RE RATHER EXTENSIVE, SO I WON'T TRY TO DESCRIBE THEM ALL DURING THIS PRESENTATION. NEXT SLIDE PLEASE.

SO LET ME JUST STOP THERE. IF THERE'S ANY QUESTIONS. I MENTIONED EARLIER WE'VE DONE EXTENSIVE

EVALUATION. WE HAVE A PRETTY GOOD UNDERSTANDING OF HOW INSTITUTIONS IMPLEMENTED, AND WE'VE DONE A SET OF COMPLIANCE EVALUATIONS IN TERMS OF THE IMPLEMENTATION OF THESE REGULATIONS. SO OUR UNDERSTANDING IS THEY'RE EFFECTIVE. ALL OF OUR INSTITUTIONS HAVE EFFECTIVE PROCEDURES AND POLICIES FOR IMPLEMENTING THEM. IF THERE'S ANY QUESTIONS ON THE SPECIFICS OF THE REGULATIONS, I'M HAPPY TO TAKE THEM NOW. OTHERWISE, I'LL MOVE INTO THIS FINAL DISCUSSION WHICH IS SORT OF THINKING ABOUT CONTEMPORARY TOPICS. THE DAY IS WEARING ON.

SO THE FINAL PIECE WE WANTED TO DISCUSS IS -- TODAY'S DISCUSSION WAS TERRIFIC. WE'VE FOCUSED ON ONE FAIRLY LIMITED ASPECT OF THE RESEARCH WHICH IS MORE AROUND THE CLINICAL RESEARCH. BUT WITHIN THE MORE BASIC AND DISCOVERY RESEARCH SIDE, THERE ARE ONGOING ISSUES THAT WE, AGAIN, CONTINUE TO MONITOR AND WE THINK ARE IMPORTANT. THE HUMAN GENOME EDITING INITIATIVE, THE CONTINUED DEVELOPMENT OF EMBRYO MODEL SYSTEMS, THE DEVELOPMENT OF HUMAN NEURAL ORGANOIDS, SORT OF BRAINS IN A DISH IF YOU WILL. AGAIN, BLASTOCYST COMPLEMENTATION RESEARCH. IN ADDITION TO ISSUES AROUND GENETIC DATA SHARING AND PRIVACY, UNAUTHORIZED TREATMENTS TO UNAPPROVED TREATMENTS OR HIGH COST STEM CELL TREATMENTS WITH NO

CLEAR SAFETY AND EFFICACY. AND ALSO SOME DISCUSSION CAME UP AROUND CORD BLOOD BANKING AND THE EFFICACY OF CORD BLOOD BANKING. MAINLY FROM A FINANCIAL STANDPOINT IN TERMS OF WHAT THAT -- SO THOSE LAST TWO ACTUALLY HAVE SORT OF CONSUMER SORT OF PROTECTION ASPECTS, IF YOU WILL.

SO THESE ARE ITEMS THAT WE, AGAIN, CONTINUE TO TRACK. I SORT OF MAKE THE COMMENT FREQUENTLY WE'RE SORT OF ONE JOURNAL ARTICLE AWAY FROM SOME INTERESTING NEW ETHICS DISCUSSION BECAUSE SOMETHING COMES UP IN THESE SORT OF GENERAL CATEGORIES. BUT WE WANTED TO ASK THE GROUP TO WHAT EXTENT THESE ISSUES ARE -- THERE ARE ISSUES ON THE HORIZON THAT THEY THINK MIGHT BE IMPLICATED OR MIGHT NEED TO CONSIDER WITHIN THIS WORKING GROUP. SO WANTED TO KIND OF OPEN UP THAT DISCUSSION AND ASK EITHER J.T. OR THE CO-CHAIRS TOO IF THEY'D LIKE TO ADD SOME COLOR TO THIS SLIDE.

CO-CHAIRMAN KAHN: I CAN START. THE IDEA, I THINK, WAS A LITTLE PRIMING OF THE PUMP. SO AS GEOFF SAID, IN PREPARATION FOR THIS MEETING, GEOFF AND FRED AND J.T. AND I HAVE HAD NUMEROUS CONVERSATIONS. AND THESE ARE THE THINGS THAT SORT OF PERCOLATED TO THE TOP. BUT THE QUESTION FOR THE GROUP IS WHETHER MANY OF THESE REALLY FEEL LIKE

IMPORTANT THINGS TO CONTINUE TO TAKE ON AND/OR OTHER THINGS THAT WE DON'T HAVE ON THIS LIST THAT ARE WORTH ADDING TO A LIST OF TOPICS THAT WE CAN TAKE ON IN THE COURSE OF OUR FUTURE MEETINGS. NOT MEANT TO DIVE INTO ANY OF THEM NOW. REALLY A KIND OF BEGINNING OF A LIST OF ISSUES FOR US TO ADDRESS AS A GROUP.

I TALKED LONG ENOUGH FOR J.T. TO RAISE HIS HAND.

DR. FISHER: OH, GOOD. I'LL GO AFTER J.T.

CO-CHAIRMAN KAHN: J.T., YOU'RE MUTED. WE'RE STILL HAVING A PROBLEM HEARING YOU. CAN YOU COME IN THROUGH THE PHONE CONNECTION?

DR. FISHER: JUST TURN OFF YOUR COMPUTER AUDIO, YOUR COMPUTER SPEAKERS OFF, AND WE WON'T GET FEEDBACK.

CHAIRMAN THOMAS: DOES THAT WORK?

CO-CHAIRMAN KAHN: THERE YOU GO.

CO-CHAIRMAN FISHER: THAT WORKS.

CHAIRMAN THOMAS: SORRY FOR ALL THIS TECHNOLOGICAL CHALLENGES.

SO THE IDEA HERE IS THE TECHNOLOGY IS ALWAYS DEVELOPING TO DO NEW THINGS. AND OVER THE YEARS CIRM HAS GRAPPLED WITH THOSE ISSUES AS THEY HAVE ARISEN. SO THE POINT OF THIS SLIDE WAS ARE

THERE TOPICS THAT THE WORKING GROUP SEES EITHER CURRENTLY OR IN THE OFFING THAT WOULD BE GOOD SUBJECT MATTER FOR A DISCUSSION AT THE NEXT MEETING SEVERAL MONTHS DOWN THE ROAD.

SO WHAT GEOFF HAS PUT UP HERE IS SORT OF SOME OF THE ISSUES THAT WE ARE LOOKING AT AT THIS POINT; BUT ARE THERE, PARTICULARLY IN THE SCIENTIFIC REALM, ARE THERE TECHNIQUES THAT WARRANT DISCUSSION FOR THIS WORKING GROUP OR THINGS THAT YOU SEE COMING DOWN THE PIKE YOU MIGHT ANTICIPATE. SO THAT'S WHAT WE ARE LOOKING FOR HERE.

CO-CHAIRMAN KAHN: THANKS. WANT ME TO FIELD, GEOFF, OR YOU WANT TO DO IT?

DR. LOMAX: GO AHEAD.

CO-CHAIRMAN KAHN: ACCORDING TO THE WAY I SEE IT, IT LOOKS LIKE AKSHAY AND BENHUR, AND I THOUGHT FRED HAD HIS HAND RAISED EARLIER. MAYBE HE'LL COME BACK. AKSHAY, GO AHEAD.

DR. SHARMA: SO I THINK THIS IS A GREAT LIST HERE. THERE'S ALWAYS THIS CONTROVERSIAL TOPIC OF GERMLINE GENOME EDITING THAT WE MENTION, BUT WE SKIRT AROUND IT. WE NEVER ACTUALLY GET TO DISCUSSING IT. AND IT SEEMS LIKE WE HAVE SUCH A DIVERSE GROUP OF FOLKS OVER HERE WHO THIS TOPIC SEEMS RIPE FOR DISCUSSION. OF COURSE, I WOULDN'T

PUT IT ON THE TOP OF THIS LIST, BUT SOMEWHERE AT THE VERY BOTTOM IN THE END ONCE WE HAVE TACKLED ALL THESE OTHER TOPICS.

I'D LIKE TO SUGGEST THAT WE ALSO TALK ABOUT WHAT ARE THE IMPLICATIONS AND IF AT ALL EVER GERMLINE GENOME EDITING WOULD BE SOMETHING THAT WE WOULD CONSIDER.

THIS HAS CERTAINLY HAPPENED. WE ALL HAVE HEARD OF THAT CHINESE INVESTIGATOR WHO DID THE GERMLINE GENOME EDITING TO PEDIATRIC PATIENTS OR TO EMBRYOS FOR PREVENTION OF HIV. SO CERTAINLY IT'S NOT SCIENCE FICTION. AND I WOULD SAY, IF THERE ARE THESE CONTROVERSIAL TOPICS, IT WOULD BE WORTHWHILE TO DISCUSS THEM AND TO FIGURE OUT IF AND WHEN SUCH A THING MIGHT BE REASONABLE TO DO EVEN THOUGH THE REGULATIONS DON'T ALLOW FOR THAT CURRENTLY. BUT COULD THAT OR SHOULD THAT BE CHANGED IN THE FUTURE? AND I THINK IT'S WORTH HAVING THAT DISCUSSION.

CO-CHAIRMAN KAHN: COULD I JUST ADD ON TO THAT. SO THE NAS HUMAN GENOME EDITING INITIATIVE INCLUDES THAT TOPIC. IT HAS OVER THE LAST TWO TIMES THERE'S BEEN AN INTERNATIONAL MEETING. AND THE THIRD -- THEY'RE SUPPOSED TO BE EVERY OTHER YEAR, BUT THEY GOT OFF CYCLE BECAUSE OF THE PANDEMIC. BUT THE THIRD MEETING WILL BE, I THINK, IN MARCH IN

LONDON WHERE THAT CONTINUES TO BE A TOPIC OF CONVERSATION, AKSHAY, BUT WORTH SORT OF MAKING CLEAR THAT THAT IS INCLUDED IN WHAT'S HAPPENING ALL AROUND GENOME EDITING.

I WOULD MAKE A FRIENDLY AMENDMENT AND SAY HERITABLE GENETIC CHANGE OR MODIFICATION BECAUSE MITOCHONDRIAL TRANSPLANT AND TECHNIQUES SOMETIMES ARE NOT CONSIDERED GERMLINE MODIFICATION, BUT ARE CERTAINLY HERITABLE GENETIC MODIFICATIONS. AND SO THAT'S A BROADER WAY OF CATEGORIZING, I THINK, THE GENERAL ISSUE. SO HOPEFULLY YOU WOULD AGREE WITH THAT.

BENHUR.

DR. LEE: I WAS JUST GOING TO MENTION WE'RE PROBABLY NOT THERE YET SINCE WE'RE TRYING TO GET THERAPIES, ENHANCEMENTS INTO THE CLINIC. BUT IN THE HORIZONS, THAT TALKS ABOUT NEURAL AUGMENTATIONS OR STEM CELL AUGMENTATIONS FOR MUSCLE REGENERATION THAT GOES BETTER THAN CURING MUSCULAR DYSTROPHY, BUT MAKING PEOPLE MORE MUSCULAR, HAVING ATHLETES. THAT'S PERCOLATING ON THE HORIZON AND MAY OR MAY NOT BE SOMETHING THAT THE COMMITTEE WANTS TO TACKLE.

CO-CHAIRMAN KAHN: GEOFF OR AND OTHERS AT CIRM, NOWHERE IN THE MATERIALS I'VE SEEN IS THERE ANY COMMENT ABOUT ENHANCEMENT TECHNOLOGIES. DOES

THAT LIVE ANYWHERE IN THE POLICIES?

DR. LOMAX: WELL, CHIME IN THERE. I'M NOT AWARE OF IT BEING ADDRESSED EXPLICITLY, BUT IMPLICITLY WE'VE TENDED TO FRAME OUR CLINICAL PROGRAMS AROUND UNMET MEDICAL NEED. SO I THINK IN THE EVALUATION PROCESS, THE NOTION OF ENHANCEMENT MIGHT BE VIEWED WITH SOME SKEPTICISM AS AN UNMET MEDICAL NEED. SO IT'S INDIRECTLY ADDRESSED THROUGH OUR EVALUATION PROCEDURES, BUT OBVIOUSLY WOULD INVITE COMMENT FROM MY CIRM COLLEAGUES IF THEY HAVE ANYTHING TO ADD TO THAT.

CO-CHAIRMAN KAHN: JUST NOTING THAT DEFINING ENHANCEMENT OR DISTINGUISHING ENHANCEMENT FROM UNMET MEDICAL NEED IS NOTORIOUSLY CHALLENGING. MODIFYING IMMUNE RESPONSE IS SOME WAY AN ENHANCEMENT, BUT ALSO SEEMS LIKE IT SOLVES AN UNMET MEDICAL NEED. SO A REALLY INTERESTING SPACE. SO I APPRECIATE BENHUR'S SUGGESTION HERE.

I DON'T SEE ANY OF OUR CIRM COLLEAGUES WANTING TO WEIGH IN ON THIS. SO IF NOT, CHRIS, YOU'RE NEXT.

DR. SAHA: I ALSO THINK ENHANCEMENT IS AN INTERESTING BUT THORNY TOPIC.

THE OTHER THING THAT CAME UP IN MY MIND IS IN UTERO GENE THERAPY AND GENE EDITING. THERE'S

CERTAINLY ACTIVITY IN CALIFORNIA. THERE MIGHT BE A NEED TO ESTABLISH STANDARDS THERE THAT WEIGH THE RELATIVE LIVES OF THE MOTHER AND THE FETUS. AND IT'S A QUICKLY EVOLVING SPACE.

CO-CHAIRMAN KAHN: I THINK DR. FARMER WAS GOING TO SPEAK TO SOME OF THOSE ISSUES. RIGHT, GEOFF? THAT WAS GOING TO BE INCLUDED IN THAT PRESENTATION.

DR. LOMAX: YEAH. WE CAN INVITE FOLKS BACK WHO ARE INVOLVED IN THAT WORK IF IT'S A TOPIC OF INTEREST.

CO-CHAIRMAN KAHN: ANY OTHER? THIS IS A HEALTHY LIST, AND WE'VE ADDED A FEW THINGS TO IT. SO IT'S NOT LIKE WE'RE GOING TO BE WANTING FOR TOPICS.

CO-CHAIRMAN FISHER: THE OTHER WAY TO ASK THE QUESTION: IS THERE ANYTHING THAT'S ON HERE THAT PEOPLE QUESTION OR THINK SHOULD NOT BE?

CO-CHAIRMAN KAHN: UH-HUH. I GUESS NOT. FRED, I REMEMBER WE HAD A CONVERSATION AND YOU WERE VERY INTERESTED IN THE CORD BLOOD BANKING ISSUES. I MEAN THAT'S A FAIRLY CRYPTIC HEADING THERE. MAYBE YOU WANT TO SAY TWO WORDS ABOUT WHAT YOU WERE THINKING ABOUT INCLUDING THAT TOPIC.

CO-CHAIRMAN FISHER: SURE. THE LAST THREE

ON THIS LIST ARE REALLY WHERE THE OBVIOUS CROSSOVER TO CONSUMERS TAKES PLACE, AND THINGS THAT PEOPLE WITH GENETIC DISORDERS, CERTAINLY THE PRIVACY ISSUES EXIST. THE CORD BLOOD BANKING ISSUE IS ONE THAT I'M NEWLY FAMILIAR WITH BECAUSE I'VE LEARNED HOW PEOPLE WHO ARE ABOUT TO DELIVER A BABY ARE BEING ASKED IF THEY WANT TO BANK THEIR CORD BLOOD. AND THIS ASK IS COMING THROUGH THE HOSPITALS THAT ARE PERFORMING THE DELIVERIES, BUT THE CORD BANKING IS DONE BY PRIVATE COMPANIES.

AND IT'S BASED -- I'M REMINDED OF THE PRESENTATION EARLIER TODAY WHERE IT'S SORT OF BASED ON THIS SORT OF VAGUE PROMISE THAT IF YOU BANK YOUR CORD BLOOD, YOUR KID IS GOING TO BE ABLE TO BE CURED OF DISEASES DOWN THE ROAD. AND SO YOU SHOULD DO THIS AND DO IT AT GREAT EXPENSE, WHICH IN AND OF ITSELF MEANS MANY PEOPLE WILL NOT BE ABLE TO PARTICIPATE EVEN IF THEY WANTED TO BECAUSE THEY COULDN'T AFFORD THE PRICE.

SO ACCESSIBILITY IS AN OPTION, BUT I THINK THE REAL CONFLICT IS HOW THIS IS BEING MARKETED TO PEOPLE WHO ARE AT A VERY VULNERABLE STATE. THEY'RE ABOUT TO DELIVER A CHILD. THEY'RE PROJECTING FORWARD. AND, IN ESSENCE, BY NOT DOING IT, THEY ARE POTENTIALLY DENYING THEIR CHILD A CURE THAT

OTHERWISE WOULD BE AVAILABLE TO THEM HAD THEY BANKED THEIR CORD BLOOD, WHICH IS JUST PREYING. IT SEEMS LIKE THE PREDATORY LENDING. IT'S JUST PREDATORY BECAUSE THERE'S NO EVIDENCE THAT BANKING CORD BLOOD, NO MEANINGFUL EVIDENCE, I GUESS, THAT IT'S GOING TO MAKE A HUGE DIFFERENCE AT LEAST TODAY. SO IT'S KIND OF LEVERING THE PUBLIC'S PERCEPTION THAT STEM CELL THERAPY IS GOING TO BE THE END ALL AND BE ALL AND CURE -- BETWEEN STEM CELL THERAPY AND GENE THERAPY, ALL DISEASE IS GOING TO GO AWAY. AND IF YOU DON'T PAY THIS EXORBITANT AMOUNT OF MONEY, YOU'RE BASICALLY DENYING YOUR UNBORN CHILD THE ABILITY TO BE CURED IN THE FUTURE.

SO I THINK THERE ARE LOTS OF ETHICAL QUESTIONS AROUND THAT. HOPEFULLY I'VE DONE A DECENT JOB ARTICULATING WHAT THEY ARE, BUT THAT'S REALLY WHERE THIS ISSUE IS COMING FROM. HOPEFULLY THAT WAS HELPFUL. AND I'D BE INTERESTED IN ANYBODY'S THOUGHTS ABOUT IT ONE WAY OR THE OTHER.

CO-CHAIRMAN KAHN: LARRY.

DR. GOLDSTEIN: JUST TO FOLLOW UP ON FRED'S COMMENT. THE LAST TIME I LOOKED INTO THIS ISSUE WAS ABOUT 10 OR 15 YEARS AGO WHEN I WAS WRITING A BOOK. BUT AS I UNDERSTAND THE DATA, ALMOST ALL TRANSPLANTS OF CORD BLOOD ORIGINATE AT BE

THE MATCH, WHICH IS THE PUBLIC BANK. AND IT'S VERY UNUSUAL FOR PRIVATE BANKS TO CONTRIBUTE CORD BLOOD TO THE DONOR FOR A DISEASE THAT CAN USEFULLY BY MODIFIED BY THAT CORD BLOOD. SO AS I UNDERSTAND IT, THE INDUSTRY IS ALMOST A COMPLETE RIP-OFF.

CO-CHAIRMAN KAHN: THE PERSON I WOULD CALL TO ASK THIS QUESTION IS JOHN WAGNER WHO HAPPENS TO BE RIGHT BELOW GEOFF ON MY SCREEN. I DON'T KNOW, JOHN, IF YOU WOULD CARE TO OPINE ABOUT THIS.

DR. WAGNER: WELL, AS LARRY IS JUST MENTIONING, THIS HAS BEEN A LONGSTANDING CONTROVERSY. AND IT'S NOT TO SAY THAT IT'S NOT WORTH REVISITING, BUT IT'S NOT A NEW ISSUE. AND THERE HAVE BEEN MANY ARTICLES WRITTEN ON THIS TOPIC ABOUT WHETHER YOU SHOULD OR SHOULD NOT, WHAT THE POTENTIAL IS, AND HOW LIKELY IT IS THAT YOU'D EVER BE USING IT, AND COULD IT BE USED FOR SOMETHING OTHER THAN HEMATOPOIETIC STEM CELL TRANSPLANTS? THE ANSWER IS PROBABLY, YES, IT COULD BE. BUT STILL I DON'T THINK ANYTHING IS PROVEN TO BE ABLE TO SAY, YES, THIS IS WORTHWHILE OR NOT.

ALTHOUGH I'M USING THE PUBLIC BANK, THEORETICALLY I GUESS YOU COULD GO AND TELL PEOPLE THAT YOU COULD CREATE, FOR EXAMPLE, REGULATORY T-CELLS AS A WAY OF CONTROLLING AUTOIMMUNE DISEASE

OR GRAFT VERSUS HOST DISEASE, OR HOWEVER YOU WANT TO DO IT. I'M NOT SAYING THAT'S WHAT YOU SHOULD DO. BUT SINCE MY OWN RESEARCH IS USING CORD BLOOD AS A SOURCE OF REGULATORY T-CELLS AS A WAY OF CONTROLLING SOME OF THESE COMPLICATIONS, I GUESS YOU COULD CREATE AN AUTOLOGOUS PRODUCT. YOU CAN IMAGINE ALL THE CHALLENGES THAT WOULD BE TO MAKE IT -- FIRST OFF, IT'S GOING TO BE MUCH MORE COSTLY TO MAKE THE INDIVIDUALIZED PRODUCT RATHER THAN MAKING A BANK OF THESE CELLS. THERE COULD BE ADVANTAGES, BUT I'VE NEVER TRIED TO STUDY AUTOLOGOUS VERSUS ALLOGENEIC AS A STARTING CELL SOURCE.

BUT TO BE A HONEST WITH YOU, IT'S NOT A TOPIC THAT I'M PARTICULARLY INTERESTED IN REVISITING, NOT TO SAY THAT THE GROUP SHOULDN'T DO IT. IT'S JUST THAT IT'S BEEN DONE OVER AND OVER AGAIN, BUT MAYBE THERE'S A NEW TWIST.

CLEARLY WHAT WOULD BE GREAT IS IF WE CAN GET REAL DATA FROM THE AUTOLOGOUS CORD BLOOD BANKS AND SAY, "TELL US WHAT YOU'VE DONE. HOW DO YOU JUSTIFY THIS?" BUT IN THE PAST IT WAS REALLY A STRUGGLE GETTING THAT INFORMATION FROM THEM. SO WHAT DATA CAN WE BRING TOWARDS THIS THAT'S DIFFERENT THAN WHAT WE ALREADY HAVE DONE IN THE PAST? I JUST DON'T KNOW.

CO-CHAIRMAN FISHER: SO I'LL TRY TO RESPOND AT LEAST FROM A CONSUMER POINT OF VIEW. GIVEN THAT CIRM IS IN THE BUSINESS OF STEM CELL AND GENE THERAPY, THERE'S STRONG OVERLAP BETWEEN THE PEOPLE WHO ARE BEING ENCOURAGED AT THE CONSUMER LEVEL TO BANK THEIR BLOOD AT HIGH COST AND THE BUSINESS THAT CIRM IS IN. AND WHILE THERE MIGHT HAVE BEEN -- I'LL JUST SAY THERE HAVE BEEN -- WHILE THIS ISSUE HAS BEEN LOOKED AT A LOT BY OTHERS, THAT KNOWLEDGE AND ANY CONCLUSIONS THAT COME FROM THAT ANALYSIS HASN'T BEEN WIDELY SHARED WITH THE CONSUMER COMMUNITY.

AND SO CIRM MAY HAVE A ROLE IN COMING UP WITH A POLICY RECOMMENDATION JUST LIKE THIS GROUP MAY COME UP WITH POLICY RECOMMENDATIONS ON OTHER ISSUES. CIRM MAY CHOOSE TO AND THIS GROUP MAY RECOMMEND THAT CIRM TAKE A POSITION THAT IT CAN SHARE WITH CALIFORNIA CONSUMERS TO INFORM THEIR CHOICES ABOUT THIS BECAUSE CONSUMERS WOULD HAVE TO GO THROUGH A LOT OF WORK TO DO THEIR OWN ANALYSIS. AND MOST OF THE TIME THEY'RE DOING THAT WORK IN THE MIDST OF WHAT BECOMES AN EMOTIONAL CRISIS.

SO I'M NOT DOUBTING ANYTHING THAT YOU'RE SAYING, BUT TRYING TO FRAME IT IN THE CONTEXT OF HOW THIS MIGHT BE A TOPIC FOR THIS GROUP IN THE CONTEXT

OF PROVIDING SOME ADVICE TO CIRM AROUND IT.

CO-CHAIRMAN KAHN: HELPFUL. THANK YOU.

LARRY, I SEE YOUR HAND IS JUST UP FROM BEFORE. SO IF THAT'S RIGHT, THEN WE CAN GO TO MARIA.

DR. MILLAN: ON THAT TOPIC, WOULD IT BE HELPFUL IF THE CIRM TEAM PROVIDES KIND OF A SUMMARY OF WHAT TYPES OF PROJECTS MAY USE UMBILICAL CORD BLOOD BECAUSE WE REALLY HAVE VERY FEW PROJECTS, AS FAR AS I KNOW, BUT WE CAN LOOK AT WHICH ONES WE DO HAVE. AND THEN IF THERE'S SOME SORT OF CONCERN, SPECIFIC CONCERN RELATIVE TO THE TOPIC OF BANKING CORD BLOOD, THEN THAT COULD BE SOMETHING THAT CAN INFORM THE CONVERSATION MAYBE. SO IT WOULD BE HELPFUL IF THE TEAM BRINGS BACK SOME INFORMATION REGARDING THE CIRM PORTFOLIO.

DR. WAGNER: I THINK THE OTHER THING TO KEEP IN MIND WHERE THERE'S BEEN A LOT OF PUBLICITY RELATED TO THIS HAS BEEN ARE YOU USING CORD BLOOD IN THE SETTING OF PATIENTS WITH PERINATAL LOW OXYGENATION RESULTING IN CEREBRAL PALSY AND OTHER CASES DOING STUDIES LOOKING AT IMPACT UPON YOUNG CHILDREN WHO HAVE SEVERE MANIFESTATIONS OF AUTISM AND A VARIETY OF OTHER CONDITIONS. AND THE WORK IS PRIMARILY BEING DRIVEN BY JOANNE KURTZBERG AT DUKE

UNIVERSITY. BUT THESE ARE VERY COMMON DISEASES AND SO GETS A LOT OF PUBLICITY. AND THERE ARE PEOPLE THAT ARE BELIEVERS AND THERE ARE PEOPLE WHO ARE NOT BELIEVERS.

THAT'S A PATH THAT -- FIRST OFF, WHAT WOULD BE INTERESTING IS TO DETERMINE WHETHER OR NOT, IN DIFFERENT INSTITUTIONS, WHETHER OR NOT THE RESULTS WERE REPEATABLE AND IF INDEED THEY CONTINUE TO BE AS GOOD AS WHAT WAS PREVIOUSLY REPORTED. BUT WHAT'S INTERESTING IS THAT MOST CENTERS HAVE NOT JOINED ON IN TRYING TO REPLICATE IT. AND THAT COULD BE FOR SEVERAL REASONS, BUT YET WHAT YOU HEAR ABOUT IS MANY PEOPLE SAY, WELL, I JUST DON'T UNDERSTAND THE MECHANISM, SO I'M NOT GOING TO REPEAT IT. THAT MIGHT BE THE RIGHT ANSWER TOO.

IN ANY EVENT, CLEARLY IF THAT WAS -- IF ALL THAT WAS AS GOOD AS WHAT WAS INITIALLY RECORDED, THEN YOU CAN IMAGINE -- I CAN TELL YOU NOW THAT THE AUTOLOGOUS CORD BLOOD BANKING INDUSTRY, THEY RELY ON THAT DATA IN PARTICULAR. IT'S NOT BONE MARROW TRANSPLANTS. IT'S NOTHING ELSE THAT WE ORIGINALLY TALKED ABOUT. IT'S REALLY THIS IDEA THAT IT COULD BE BENEFICIAL IN AUTISM AND OTHER NEUROLOGICAL DISORDERS.

SO WE'D HAVE TO DO A DEEP DIVE INTO THAT

PERHAPS, BUT THAT'S REALLY WHERE THE MOST INTEREST HAS BEEN. I HAVE NO SPECIFIC EXPERIENCE IN IT TO BE ABLE TO ADD MY OWN EXPERIENCE WITH THAT, BUT OTHERS MIGHT HAVE THOUGHTS ABOUT THAT.

CO-CHAIRMAN KAHN: I GUESS THE OTHER SIDE OF THIS COIN, ONE WAY TO THINK ABOUT IT IS LARRY'S POINT, AND, JOHN, YOU KNOW THIS WORLD VERY WELL TOO, IS DONATION OF CORD BLOOD TO PUBLIC BANKS. SO BE THE MATCH OR WHAT USED TO BE THE NATIONAL MARROW DONOR PROGRAM. AND THE QUESTION IS REALLY HAS CIRM EVER TAKEN A POSITION OR MADE RECOMMENDATIONS TO THE PUBLIC ABOUT THE IMPORTANCE AND NEED FOR PEOPLE TO DONATE CORD BLOOD AFTER BIRTH? RATHER THAN PAYING TO BANK THEM FOR PERSONAL USE, DONATING THEM FOR OTHERS TO HAVE ACCESS TO FOR THERAPEUTIC PURPOSES. HAS THERE EVER BEEN A POLICY DISCUSSION ABOUT THAT?

DR. WAGNER: CERTAINLY THE AMERICAN ACADEMY OF PEDIATRICS HAS.

CO-CHAIRMAN KAHN: RIGHT. MEANING FROM CIRM.

DR. WAGNER: I KNOW WHAT YOU MEAN.

DR. LOMAX: NONE THAT I'M AWARE OF AS A SPECIFIC RECOMMENDATION. THAT WOULD HAVE TO COME FROM OUR BOARD TYPICALLY AS A POLICY RECOMMENDATION.

DR. MILLAN: IT HASN'T REALLY BEEN A BIG

PART OF OUR PORTFOLIO, AND IT HASN'T ARISEN THAT OFTEN FOR A PROGRAM SPECIFIC. BUT IT WOULD BE INTERESTING TO LOOK AT HOW CORD BLOOD, IN TERMS OF THE DISCOVERY, TRANSLATION, OR EVEN CLINICAL PROGRAMS, WHAT TYPE OF ACTIVITY WE HAVE WITHIN OUR PORTFOLIO. AND WE CAN HAVE A QUICK LOOK AT THAT AND BE BACK TO THIS GROUP TO TAKE A LOOK AT IT AND SEE IF THERE'S ANYTHING ABOUT THAT THAT MAY SPARK INTEREST IN A PARTICULAR ASPECT OF THIS QUESTION.

BUT I THINK THAT THE TOPIC ABOVE THAT IN TERMS OF STEM CELL TOURISM, DIRECT TO CONSUMER IS A VERY IMPORTANT TOPIC THAT WE HAVEN'T REALLY BEEN ABLE TO REALLY ADDRESS. AND IT REALLY DOES SPEAK TO YOUR CONCERN, FRED, IN TERMS OF PROTECTING THE PUBLIC FROM MISUSE OF A RATIONALE TO BE EXPLOITED.

OF COURSE, CIRM DOES WHAT IT CAN TO EDUCATE THE PUBLIC. WE HAVE THINGS ON OUR WEBSITE, AND WE ATTEMPTED TO HAVE CONVERSATIONS MEDIATED BY SENATOR TORRES WITH OUR MEDICAL BOARD, BUT WE HAVEN'T REALLY MADE ANY HEADWAY IN TERMS OF SPECIFIC POLICY OR RECOMMENDATIONS ABOUT HOW WE CAN PROTECT AGAINST DIRECT TO CONSUMER EXCEPT FOR BRINGING AWARENESS TO IT.

CO-CHAIRMAN KAHN: LEONDRA, I SEE YOUR HAND.

DR. CLARK-HARVEY: YES. THANK YOU. I JUST HAD A QUESTION MORE ABOUT PROCESS AND PROCEDURE AND MAYBE HISTORY. I HEARD THE RECOMMENDATION IT SOUNDED LIKE OR QUESTION AROUND IF CIRM HAS IN THE PAST PUT OUT STATEMENTS OR EVEN, IT SOUNDED LIKE, A POLICY SUGGESTION. I'M JUST WONDERING, AS IT PERTAINS TO THIS PARTICULAR ISSUE, BUT HAS CIRM DONE THAT IN THE PAST? AND WHAT IS THE APPROPRIATENESS AND THE CHARGE OF CIRM IN DOING THAT? I'M JUST WONDERING ABOUT, AS WE TALK ABOUT ETHICS, I'M JUST WONDERING HAVE WE DONE THAT ON OTHER ISSUES AND MADE RECOMMENDATIONS? WHAT'S OUR TRACK RECORD THERE? AND THEN IS THAT APPROPRIATE FOR US TO DO?

DR. LOMAX: THE EFFORTS THAT I'M AWARE OF, AS MARIA ALLUDED TO, WE DID DO A PRESENTATION TO THE MEDICAL BOARD, AND WE HAVE DONE A PUBLICATION ADVOCATING THAT STEM CELL TREATMENTS FOR PATIENTS MEET CERTAIN CRITERIA. AND THOSE ARE THE CRITERIA WHICH WE APPLY, WHICH IS THAT THEY ARE UNDER AN FDA IND AND THEY'RE BEING DELIVERED UNDER APPROPRIATE SCIENTIFIC RIGOR SO THAT THEY'RE BEING EVALUATED FOR EFFICACY OR WHATEVER THE ENDPOINT IS UNDER THAT IND.

SO TO THE EXTENT WE HAVE A PUBLIC ARTICULATION OF THAT IN A SORT OF POLICY-RELATED FRAMEWORK, THERE'S ONE PUBLICATION THERE IN

PARTICULAR THAT WE HAD PUBLISHED, I THINK, ABOUT FOUR YEARS AGO. BE HAPPY TO CIRCULATE IT TO THE GROUP BECAUSE PERHAPS IT WOULD GIVE YOU A SENSE OF HOW WE'VE ATTEMPTED TO ARTICULATE POLICY POSITIONS. AGAIN, THAT WAS UNDER THE GUIDANCE OF SENATOR TORRES. SO IT'S COMING THROUGH OUR LEAD LEGISLATIVE REPRESENTATIVE ON THE BOARD.

DR. CLARK-HARVEY: I APPRECIATE THAT. I THINK THAT MAKES SENSE TO ME. THAT'S REALLY AROUND -- TO ME THAT'S VERY JUSTIFIABLE AROUND ETHICS AND THE SCIENCE TO BACK THAT UP. BUT IN TERMS OF THE RECOMMENDATION KIND OF BROACHED A MINUTE AGO AROUND MAYBE NOT JUST RECOMMENDING THE, AND MAYBE I HEARD IT WRONG, BUT STEM CELL CORD USE YOURSELF, BUT FOR OTHER PEOPLE IN DONATION, THAT, I THINK, IS A LITTLE DIFFERENT. AND SO THAT'S WHERE MY QUESTION KIND OF COMES FROM. I HOPE THAT MAKES SENSE.

CO-CHAIRMAN KAHN: YEAH. I WASN'T SUGGESTING WE MAKE SUCH A RECOMMENDATION. I WAS JUST ASKING ABOUT ADVOCACY IN PARTICULAR TOPICS, THAT ONE BEING THE EXAMPLE. YOUR QUESTION IS A VERY GOOD ONE.

DR. CLARK-HARVEY: YEAH. I THINK THAT ACTUALLY IS A GOOD QUESTION, BUT IT JUST BRINGS ME

TO KIND OF LIKE WHAT'S OUR ROLE AND OUR POSITION, AND IS THAT A RECOMMENDATION FOR US TO MAKE? IF SO, GREAT. BUT I'M JUST GENUINELY CURIOUS ABOUT THAT, SO WOULD APPRECIATE SOME BACKGROUND INFORMATION THERE. THANKS FOR YOUR PATIENCE.

CO-CHAIRMAN FISHER: I THINK THE OTHER SORT OF PIECE OF THIS DYNAMIC IS THAT THE INSTITUTIONS THAT ARE, IN ESSENCE, HOPING TO MARKET THESE PRIVATE CORD BLOOD BANKS ARE INSTITUTIONS THAT CIRM FUNDS FOR STEM CELL RESEARCH. I DON'T KNOW IF THAT PRESENTS A CONFLICT OF INTEREST OR NOT BECAUSE THE EFFORTS SEEM TO BE ENTIRELY SEPARATE FROM ONE ANOTHER. BUT GUIDANCE FOR THE CONSUMER COMMUNITY, I THINK, WOULD BE VERY HELPFUL. AND I DON'T KNOW WHERE ELSE THEY WOULD GET THAT OTHER THAN FROM THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE.

CO-CHAIRMAN KAHN: I SEE LARRY AND MARIA'S HANDS. LARRY, GO AHEAD.

DR. GOLDSTEIN: JUST A QUICK RESPONSE TO FRED. MANY SCIENTIFIC AND MEDICAL SOCIETIES DO PUBLISH PAPERS AND POSITION PAPERS ON THESE TOPICS. I WONDER IF A MIDDLE GROUND IS FOR CIRM TO LINK TO THOSE SORTS OF POSITION PAPERS AS A SERVICE TO THE PUBLIC BY CURATING THAT SORT OF INFORMATION.

CO-CHAIRMAN KAHN: MARIA. FRED, YOU WANT

TO RESPOND, GO AHEAD.

CO-CHAIRMAN FISHER: I THINK THE LIST WAS PUT UP THERE JUST AS SORT OF A HERE'S WHAT WE'VE BEEN THINKING. RESPOND TO WHETHER THESE ITEMS ON THIS LIST ARE RELEVANT OR NOT RELEVANT OR WHAT ELSE WOULD YOU ADD TO IT AND THAT WE WEREN'T GOING TO BE TAKING A DEEP DIVE INTO RESOLVING THE ISSUE. AND LARRY'S SUGGESTION, WHICH IS AN INTERESTING ONE, IS SOMETHING THAT I THINK POTENTIALLY COULD COME OUT OF WHATEVER THIS GROUP'S PROCESS WOULD BE AROUND THIS ISSUE.

SO NOT DISREGARDING WHAT LARRY SAID AT ALL, BUT JUST TRYING TO REFOCUS OR BE CLEAR ABOUT WHAT IT IS WE WANT TO ACCOMPLISH VIA THIS CONVERSATION TODAY BECAUSE I DON'T THINK IT'S THAT WE WANT TO RESOLVE THE ISSUE NECESSARILY ONE WAY OR THE OTHER.

CO-CHAIRMAN KAHN: YES. IT OBVIOUSLY RELATES TO YOUR POINT ABOUT UNAPPROVED STEM CELL TECHNOLOGIES, THAT THEY ARE KIND OF ALL OF A PIECE. SO MAYBE THAT'S HOW WE SORT OF CAPTURE THIS FOR FUTURE CONVERSATION.

MARIA, I SEE YOU NODDING. YOUR HAND'S UP TOO, SO GO AHEAD.

DR. MILLAN: I AGREE WITH THAT. ONE OF

THE THINGS AS A SEPARATE TOPIC, JUST FOLLOWING ON WHAT FRED FISHER HAD JUST MENTIONED, THE TOPIC OF ENHANCEMENTS I THINK IS A VERY IMPORTANT TOPIC BECAUSE LONGEVITY RESEARCH, FRAILTY RESEARCH, THOSE ARE THINGS THAT ARE KIND OF ON THE CUSP HERE. AND IT'S KIND OF THIS FUZZY AREA, BUT THAT THERE'S SOME SCIENCE BEHIND MECHANISTICALLY IN TERMS OF MOLECULAR MECHANISMS TO RESET AND KIND OF RESET CLOCKS AND THINGS LIKE THAT, THOSE ARE VERY HOT TOPICS RIGHT NOW IN THE SCIENTIFIC ARENA. SO I WANTED TO JUST SUPPORT THAT THAT IS AN IMPORTANT TOPIC, I THINK, FROM THE CIRM PORTFOLIO AND THE TYPES OF PROGRAMS WE SEE THAT MAY BE COMING IN.

CO-CHAIRMAN KAHN: I GUESS ALTOS LABS BEING THE REFERENCE THERE.

DR. MILLAN: I'M SORRY.

CO-CHAIRMAN KAHN: ALTOS BEING THE KIND OF REFERENCE. IS THAT WHAT YOU MEAN?

DR. MILLAN: THERE ARE DEFINITELY -- IT'S A WHOLE DERIVATION OF WHAT'S HAPPENED WITH IPS REPROGRAMMING. UTILIZATION FOR JUST REPROGRAMMING US IN TERMS OF -- IT'S NOT A VALUE JUDGMENT. IT'S JUST THAT IT IS ACTUALLY A VERY INTERESTING SCIENTIFIC DIRECTION. AND THAT DIVISION BETWEEN HEALTHY LONGEVITY AND ENHANCEMENT, IT IS A VERY, AS

I THINK YOU POINTED OUT, IT'S A BLURRY KIND OF SITUATION OFTENTIMES WHEN YOU'RE EVALUATING. IS THIS TRULY ENHANCEMENT OR ARE YOU ADDRESSING A TRUE UNMET NEED?

CO-CHAIRMAN KAHN: I WAS MAKING REFERENCE TO THE FACT THAT I THINK AMONG THE LEADING EFFORTS THAT ARE HAPPENING IN CALIFORNIA, BUT IN THE PRIVATE SECTOR, I THINK. I DON'T THINK ANY OF THAT IS HAPPENING IN PUBLIC UNIVERSITIES. J.T.

CAN'T HEAR YOU AGAIN.

CHAIRMAN THOMAS: I WAS SAYING IN RESPONSE TO LEONDRA'S QUESTION ABOUT PROCESS, I THINK THAT THE POSITIONS THAT CIRM TAKES ON VARIOUS THINGS ARE SORT OF CASE BY CASE, AND IT GETS KIND OF TRICKY. SO ON THE STEM CELL CLINIC ISSUE, FOR EXAMPLE, WE ARE ABLE TO EXPRESS OUR OPINION AS WE DID TO THE MED BOARD, BUT WE ARE SORT OF TAKING A BACK SEAT TO EFFORTS THAT THE FDA HAS TO TAKE TO ACTUALLY DO SOMETHING FROM A REGULATORY STANDPOINT ABOUT ENFORCING WHAT -- TAKING ACTIONS AGAINST THESE CLINICS LIKE THE ONE IN FLORIDA THAT INJECTED THE STEM CELLS INTO THE WOMEN'S EYES AND CAUSED BLINDNESS, ET CETERA. WE CAN TAKE A POSITION AS TO THE ETHICAL ASPECT OF THAT. BUT IN TERMS OF ACTUALLY BEING ABLE TO DO SOMETHING IN THAT ARENA,

WE ARE A BIT HAMSTRUNG AND AT THE MERCY OF WHAT THE FDA DOES. AND WE OBVIOUSLY CAN ENCOURAGE THE FDA TO TAKE A MORE PROMINENT ROLE THAN THEY HAVE TO THIS POINT IN CRACKING DOWN ON STEM CELL CLINICS.

BUT AS A GENERAL MATTER, I THINK MANY TIMES WHEN THESE TOPICS COME UP, WE WILL DISCUSS THEM, BUT WE ARE ALSO PART OF A LARGER DIALOGUE THAT WILL GO ON ON ETHICAL ISSUES. FOR EXAMPLE, ON THE GERMLINE GENE EDITING ISSUE, WHEN IT SPRUNG UP SEVERAL YEARS AGO AND GENERATED INTERNATIONAL OUTCRY, THE ISSCR CAME OUT WITH REGULATIONS THEY WERE PROPOSING, ET CETERA. I THINK THAT WE HAD AN ACTIVE VOICE IN THAT DIALOGUE, WHICH IS SOMETHING THAT'S ENTIRELY APPROPRIATE FOR US TO DO.

WHAT WE DO ON INDIVIDUAL ISSUES GOING FORWARD, I THINK WE NEED TO HAVE THAT DISCUSSION PER ISSUE. I THINK IT'S A GREAT QUESTION YOU'RE ASKING BECAUSE THERE ARE THINGS WE CAN DO AND THINGS WE CAN'T DO, AND IT VARIES ACCORDING TO WHAT THE ISSUE MAY BE.

SO WITH EACH OF THESE THINGS THAT WILL COME UP FOR FUTURE DISCUSSION, I THINK IT'S ENTIRELY APPROPRIATE TO ASK THE QUESTION: WHAT CAN CIRM DO TO ADVANCE THE DIALOGUE IN THIS SPACE? AND HOW IS THE BEST WAY TO EXPRESS THAT? SO I THINK THAT WAS A

GREAT THING TO ASK AND SOMETHING THAT WE SHOULD HAVE AS KIND OF A CHECKLIST ITEM WITH EVERYTHING WE DISCUSS GOING FORWARD.

CO-CHAIRMAN KAHN: VERY HELPFUL. THANK YOU. JOHN WAGNER.

DR. WAGNER: SO MY INITIAL POINT I WAS GOING TO MAKE IS A BIT DIFFERENT, BUT I WANT TO FOLLOW UP ON WHAT JONATHAN JUST SAID. SO I DON'T KNOW WHAT THE STATE OF THE FIELD IS NOW IN TERMS OF PURPOSEFUL GENERATION OF GAMETES FROM PLURIPOTENT STEM CELLS. BUT CLEARLY THINKING ABOUT THE PEOPLE I WORK WITH, WHICH ARE THE PEOPLE THAT HAVE UNDERGONE TRANSPLANT OR MANY COURSES OF CHEMOTHERAPY AND ARE NOW INFERTILE, HAS THE FIELD ADVANCED FAR ENOUGH WHERE THIS IS SOMETHING THAT SHOULD BE READDRESSED? MAYBE OTHERS ARE ALREADY ADDRESSING IT.

IT'S ONE THING WHEN WE'RE TALKING ABOUT SOMETHING SUCH LIKE GERMLINE EDITING, BUT THIS IS REALLY TO CREATE NORMAL GAMETES FROM THE INDIVIDUAL FROM WHICH IS NO LONGER FERTILE. AND I'M VERY NAIVE IN THIS PARTICULAR AREA OF RESEARCH, SO MAYBE I'M NOT STATING IT CORRECTLY. BUT IS THIS SOMETHING THAT'S WORTH A CONVERSATION ABOUT AGAIN MOVING FORWARD? JUST REALLY ASKING THAT QUESTION.

CO-CHAIRMAN KAHN: I THINK I MENTIONED

THIS ON OUR PRECALL YESTERDAY. THE NATIONAL ACADEMIES ARE HOSTING A WORKSHOP IN MID-APRIL ON EXACTLY THIS TOPIC. I ONLY LEARNED ABOUT IT YESTERDAY, THAT I WAS INVITED TO MODERATE ONE OF THE SESSIONS. SO IT'S AT LEAST RISEN TO THE LEVEL THAT THEY'RE THINKING IT'S IMPORTANT ENOUGH TO HOST A THREE-DAY MEETING ON BASIC SCIENCE, CLINICAL UNDERTAKING, AND ETHICS AND POLICY ISSUES. SO I THINK THE ANSWER IS YES. WE CAN CERTAINLY WATCH TO SEE WHAT COMES OUT OF THAT CONVERSATION.

ELI Y ADASHI IS CHAIRING THE MEETING. I DON'T KNOW IF YOU KNOW HIM, THE FORMER DEAN OF THE MEDICAL SCHOOL AT BROWN AND AN OB-GYN REPRODUCTIVE TECHNOLOGY SPECIALIST DURING HIS MEDICAL PRACTICE YEARS. SO THERE'S CLEARLY ATTENTION BEING PAID, AND IT MUST BE SUFFICIENTLY ADVANCED OR ADVANCING TO WARRANT THIS LEVEL OF DISCUSSION. SO WE CAN PAY ATTENTION TO AT LEAST WHAT HAPPENS THERE.

DR. WAGNER: JUST ONE FOLLOW-UP, IF I CAN, WHICH IS NOT FOLLOW-UP, BUT WHERE I WAS GOING ORIGINALLY BEFORE JONATHAN MADE SOME POINTS.

I'M NOT SURE WHAT THE CATEGORY WOULD BE, BUT WITH ALL THESE DIFFERENT STUDIES RIGHT NOW WITH HEMATOPOIETIC STEM CELLS AND GENE MODIFICATION, REGARDLESS OF WHAT THE UNDERLYING DISEASE IS, ONE OF

THE CONCERNS IS THE DEVELOPMENT OF CLONAL HEMATOPOESIS. IT'S IN A SETTING MOST COMMONLY, BECAUSE THEY'RE GENETIC DISEASES, OFTENTIMES IN YOUNGER PATIENTS. AND I GUESS THE QUESTION IS HOW DO YOU EVALUATE THE SAFETY OF THE PROCESS THAT YOU'RE DOING? AND YET WE'VE BEEN LOOKING AT GENETIC INFORMATION AT VARYING TIME POINTS AFTER THE THERAPY IS PERFORMED, BUT YET NOT KNOWING THE FULL MEANING OF WHAT THOSE RESULTS ARE. SO YOU COULD IMAGINE THAT YOU SAW SOME LOW VARIANT ALLELE FREQUENCY THAT MADE YOU CONCERNED, BUT YOU DON'T KNOW FOR SURE IF IT'S GOING MEAN ANYTHING. DO YOU REPORT IT? DO YOU NOT REPORT IT? HOW DO YOU DESIGN THAT STUDY?

I THINK THAT, AT LEAST WITH A NUMBER OF STUDIES THAT HAVE BEEN OUT THERE, THERE'S BEEN DISCUSSION ABOUT HOW YOU WOULD BEST DO THIS. I THINK PEOPLE ARE INTERESTED FROM THE SCIENTIFIC POINT OF VIEW, BUT AT THE SAME TIME HOW DO YOU PRACTICALLY DO THIS? I THINK IT COULD REALLY ADD TO THE FIELD GENERALLY TO KNOW WHAT HAPPENS TO THESE PATIENTS, PARTICULARLY IN CORPORATE SPONSORED TRIALS WHERE WHEN DO THEY DISCLOSE THE INFORMATION. CLEARLY, OF COURSE, WHEN IT'S AML OR MDS, BUT THERE ARE CHANGES THAT I THINK THAT WE ARE NOT LEARNING FROM BECAUSE OF FEAR OF HOW TO PERFORM THE STUDY.

THAT'S MY TAKE ANYWAY, AND OTHERS MAY HAVE OTHER THOUGHTS OR BETTER THOUGHTS ON IT. OR SOMETHING TO THINK ABOUT.

CO-CHAIRMAN KAHN: SOMETHING TO THINK ABOUT, SOUNDS LIKE. WELL, WE'VE BUILT A GOOD LIST AND HAD A GOOD CONVERSATION ABOUT SOME OF THE TOPICS ALREADY. GEOFF, WHAT'S LEFT FOR US TO DO?

DR. LOMAX: I THINK WE SHOULD DO ONE LAST CHECK ON IF THERE'S ANY PUBLIC COMMENT. IF THE MODERATOR, IS THERE ANYONE AT THIS STAGE WISHING TO COMMENT?

DR. MILLAN: JUST TO LET YOU KNOW DR. FARMER HAS JOINED. I DON'T KNOW IF YOU CAN SEE HER ON YOUR SCREEN.

CO-CHAIRMAN KAHN: I CAN.

DR. LOMAX: I SUGGESTED TO DR. FARMER IN AN E-MAIL I THINK WE SHOULD COME BACK TO THAT. I THINK THAT SINCE WE MOVED OFF THE AGENDA ITEM, AT THIS STAGE I THINK WE'LL COME BACK AND INVITE HER BACK. IT'S STILL A VERY MEANINGFUL TOPIC, BUT WE DO IT AT A SUBSEQUENT MEETING. SO APOLOGIES FOR ANY CONFUSION, PARTICULARLY IF IT WAS AT OUR END, BUT THE PERILS OF ONLINE MEETINGS. WE'RE PRETTY GOOD AT THEM, BUT EVERY NOW AND THEN HAVE A HICCUP.

DR. FARMER: NO WORRIES. HAPPY TO HELP IN

ANY WAY.

CO-CHAIRMAN KAHN: THANK YOU FOR COMING.

DR. LOMAX: SO I WOULD OBVIOUSLY LIKE TO OFFER THE CO-CHAIRS A CHANCE TO CLOSE THE MEETING OR INVITE THEM TO CLOSE THE MEETING. BEFOREHAND, I WOULD JUST LIKE TO INDULGE THE GROUP FOR ONE MOMENT IF I MAY BECAUSE I REALLY WANT TO ACKNOWLEDGE CHAIRMAN THOMAS AND HIS ONGOING SUPPORT AND LEADERSHIP AND EVERYTHING HE'S DONE TO MAKE THIS MEETING POSSIBLE. AND HE'S BEEN -- YOU COULDN'T ASK FOR A BETTER COLLABORATOR FROM MY PERSPECTIVE. HE'S REALLY HELPED ME COMPILE THE WORKING GROUP. I ASSUME MOST OF YOU KNOW HE WON'T BE THE CHAIRMAN AT THE NEXT MEETING, SO I REALLY, J.T., WANTED, YOUR PREFERENCE IN SPORTS TEAMS NOTWITHSTANDING, JUST OFFER YOU MY MOST SINCERE AND HEARTFELT THANKS FOR EVERYTHING YOU'VE DONE TO HELP ME IN THIS JOURNEY. SO THANK YOU.

CHAIRMAN THOMAS: THANK YOU VERY MUCH, GEOFF. IT'S BEEN A PLEASURE TO WORK WITH ALL OF YOU TODAY AND ALL THESE MANY YEARS IN DIFFERENT CAPACITIES WITH MANY OF YOU OVER TIME. I THINK THE ORGANIZATION IS IN GREAT SHAPE. AND WITH THE ONGOING KNOWLEDGE AND SUPPORT THAT ALL OF YOU GIVE TO IT, IT WILL ONLY RISE TO BIGGER AND BETTER

HEIGHTS. JEFF, THANK YOU. GEOFF LOMAX, THANK YOU FOR ALL YOU'VE DONE IN PUTTING THIS MEETING TOGETHER. I THINK IT'S BEEN A GREAT MEETING. AND JEFF AND FRED, AS CO-CHAIRS, FOR ALL YOUR INPUT PRE AND DURING THE MEETING. I THINK IT'S BEEN GREAT.

SO THANK YOU VERY MUCH FOR THE COMMENTS, GEOFF. I REALLY DO APPRECIATE IT AND LOOK FORWARD TO ROOTING YOU GUYS ON FROM AFAR DOWN THE ROAD. SO THANK YOU.

CO-CHAIRMAN FISHER: THANK YOU, J.T. YOU'RE WELCOME ANY TIME.

CO-CHAIRMAN KAHN: I WOULD SECOND THAT. I'M SORRY I DIDN'T GET TO HAVE MORE MEETINGS WITH YOU, BUT LOOKING FORWARD TO SOMEHOW CONNECTING DOWN THE ROAD. ALL RIGHT.

FRED, YOU HAVE ANY FAREWELL COMMENTS?

CO-CHAIRMAN FISHER: I CAN SAY THE WORDS EVERYONE IS LONGING TO HEAR, MEETING ADJOURNED.

CO-CHAIRMAN KAHN: THANK YOU ALL. WE'LL LOOK FORWARD TO THE NEXT MEETING. HOPEFULLY WE CAN ALL BE TOGETHER IN THE SAME PLACE.

(THE MEETING WAS THEN CONCLUDED AT 1:54 P.M.)

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 SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON JANUARY 5, 2023, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CA CSR 7152
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