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

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: FEBRUARY 21, 2023
12 P.M.

REPORTER: BETH C. DRAIN, CA CSR
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TUESDAY, FEBRUARY 21, 2023; 12 P.M.

CHAIRMAN GOLDSTEIN: SO, MARIANNE, IS THIS EVERYBODY WE EXPECT NOW?

MS. DEQUINA-VILLABLANCA: THERE IS TWO MORE THAT I'M EXPECTING; BUT IF YOU WANT TO PROCEED, WE CAN GO AHEAD.

CHAIRMAN GOLDSTEIN: I THINK WE SHOULD GET GOING.

THANK YOU, EVERYBODY, FOR JOINING US THIS MORNING AND THIS AFTERNOON TO TALK ABOUT HOW TO GO ABOUT PLANNING FOR THE ONE AND A HALF BILLION NEURO SET ASIDE. BEFORE WE DO ANYTHING SUBSTANTIVE, MARIANNE, CAN YOU CALL THE ROLL PLEASE.

MS. DEQUINA-VILLABLANCA: SURE. LEONDRA CLARK-HARVEY. MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MS. DEQUINA-VILLABLANCA: MARK FISCHER-COLBRIE.

VICE CHAIR BONNEVILLE: I SEE HIM CONNECTING TO AUDIO RIGHT NOW. SO YOU MIGHT WANT TO COME BACK TO HIM.

MS. DEQUINA-VILLABLANCA: FRED FISHER.

VICE CHAIR BONNEVILLE: HE IS ALSO CONNECTING TO AUDIO.

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MS. DEQUINA-VILLABLANCA: WE'LL COME BACK. JUDY GASSON.

DR. GASSON: HERE.

MS. DEQUINA-VILLABLANCA: LARRY GOLDSTEIN.

CHAIRMAN GOLDSTEIN: I'M HERE.

MS. DEQUINA-VILLABLANCA: DAVID HIGGINS.

DR. HIGGINS: HERE.

MS. DEQUINA-VILLABLANCA: STEVE JUELSGAARD. PAT LEVITT.

DR. LEVITT: HERE.

MS. DEQUINA-VILLABLANCA: LAUREN MILLER-ROGEN.

MS. MILLER-ROGEN: HERE.

MS. DEQUINA-VILLABLANCA: AL ROWLETT.

MR. ROWLETT: HERE.

MS. DEQUINA-VILLABLANCA: MARVIN SOUTHARD.

DR. SOUTHARD: HERE.

MS. DEQUINA-VILLABLANCA: JONATHAN THOMAS.

DR. THOMAS: HERE.

MS. DEQUINA-VILLABLANCA: KEITH YAMAMOTO. MARK FISCHER-COLBRIE.

DR. FISCHER COLBRIE: HERE.

MS. DEQUINA-VILLABLANCA: FRED FISHER.

DR. FISHER: HERE.

MS. DEQUINA-VILLABLANCA: AND YOU DO HAVE

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A QUORUM, LARRY.

CHAIRMAN GOLDSTEIN: GOOD. ALL RIGHT. THANK YOU, EVERYBODY.

SO WE POSTED THE AGENDA. THERE WILL BE A SLIGHT CHANGE IN THE ORDER. WE'LL TALK ABOUT EXTERNAL EXPERTS, WHICH IS AGENDA ITEM NO. 5, A LITTLE BIT AFTER TALKING ABOUT HOW WE INTEND TO PROCEED.

I WANT TO START US OFF WITH THE MOST ACCURATE STATEMENT OF TASK THAT WE HAVE, WHICH IS I'M JUST GOING TO READ A VERY SHORT SECTION FROM PROP 14 WHICH LAYS OUT WHAT WE'RE GOING TO BE THINKING ABOUT TODAY AND IN THE FUTURE. AND SO THE LANGUAGE GOES LIKE THIS: "DEDICATING $1.5 BILLION FOR THE SUPPORT OF RESEARCH AND THE DEVELOPMENT OF TREATMENTS FOR DISEASES AND CONDITIONS OF THE BRAIN AND CENTRAL NERVOUS SYSTEM, SUCH AS ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, STROKE, DEMENTIA, EPILEPSY, DEPRESSION, BRAIN CANCER, SCHIZOPHRENIA, AUTISM, AND OTHER DISEASES AND CONDITIONS OF THE BRAIN."

SO THAT'S A PRETTY BROAD MANDATE. THAT'S BASICALLY ALL OF THE NEURO DISEASES AND CONDITIONS THAT WE'LL NEED TO BE THINKING ABOUT.

WHAT I WANT TO DO BEFORE WE START

DISCUSSING PLANS IS I'VE ASKED SOME OF THE CIRM TEAM TO ASSEMBLE CURRENT PORTFOLIOS OF WHERE WE ARE BOTH WITH CIRM FUNDING AND WITH INDUSTRY AT LARGE IN CALIFORNIA AND BEYOND SO THAT WE GET AN IDEA OF WHERE MIGHT THERE BE HOLES, WHERE MIGHT WE WANT TO RECOMMEND MORE OR LESS EFFORT FROM CIRM, WHAT HAVE YOU.

AND SO THE FIRST PART OF PORTFOLIO REVIEW THAT I'D LIKE TO HAVE US LOOK AT IS A SUMMARY OF CIRM'S FUNDING PORTFOLIO SO WE KNOW WHAT WE HAVE DONE AND WHAT WE HAVE MISSED. AND ABLA IS GOING TO COVER THIS. SHE HAS A POWERPOINT PRESENTATION THAT WAS ALSO POSTED ON THE WEB. ABLA, ARE YOU IN ONE OF THESE GROUPS?

MS. DEQUINA-VILLABLANCA: SHE'S HERE IN THE ROOM, LARRY.

CHAIRMAN GOLDSTEIN: I HAD A MOMENT OF PANIC THERE. OKAY. GREAT. ABLA, TAKE IT AWAY PLEASE.

DR. CREASEY: THANK YOU, LARRY. THANK YOU, EVERYONE. I'M GOING TO PRESENT THE TRAN AND CLINICAL NEURO PORTFOLIO AS AN UPDATE FOR THE TASK FORCE. SO THE PRESENTATION OVERVIEW, WHICH YOU UNDOUBTEDLY HAVE SEEN, JUST COVERS A VARIETY OF TOPICS. CIRM NEUROLOGY CLASSIFICATION GLOSSARY JUST

TO PUT US ALL ON THE SAME PAGE. THE CURRENT CIRM TRAN AND CLINICAL NEUROLOGY PORTFOLIO. CIRM NEUROLOGY AWARDS WITH THE PROGRESSION EVENTS DEVELOPMENTS. AND I'LL DESCRIBE THAT IN DETAIL WHEN I SHOW THAT SLIDE. AND NEUROLOGY LANDSCAPE WITH CLINICAL HIGHLIGHTS. ESPECIALLY WHAT'S BEEN APPROVED IN THE AREA OF NEUROLOGY CELL AND GENE THERAPIES. OUR PENDING FDA DECISIONS REGARDING NEUROLOGY DRUGS THAT WE HAVE OBSERVED THROUGH THE FDA WEBSITE AND OTHERWISE. AND THEN NEUROLOGY CLINICAL TRIALS, SHAPING MEDICINE IN 2023 JUST TO GET EVERYONE EXCITED THAT NEUROLOGY CONTINUES TO BE ON THE FOREFRONT. FINALLY, CIRM KEY FINDINGS.

SO I'M NOT GOING TO GO OVER THE NEUROLOGY CLASSIFICATION GLOSSARY IN DETAIL, JUST TO SHOW YOU THAT WE ARE AWARE THAT THE WHOLE AREA CAN BE CLASSIFIED DIFFERENTLY, BUT THIS IS THE WAY THAT THE DISCOVERY TEAM, TRANSLATION, AND CLINICAL AGREED TO CLASSIFY THE GRANTS THAT WE HAVE BEEN RECEIVING FOR NEURODEGENERATION DISORDERS. AND YOU CAN READ THE DISEASE, SUCH AS ALZHEIMER'S, PARKINSON'S, ET CETERA. THE NEUROPSYCHIATRIC DISORDERS, SUCH AS SCHIZOPHRENIA, SLEEP/WAKE DISORDERS, ET CETERA.

AND THEN NEURODEVELOPMENTAL DISORDERS SUCH AS AUTISM, STEREOTYPIC MOVEMENT DISORDER, ET CETERA.

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AND THE REST ARE CLEAR. TRAUMATIC BRAIN INJURIES, SOME EYE DISEASE, ESPECIALLY THE RETINA AND OPTIC NERVE, DISEASES THAT AFFECT OTHER SENSORY INPUTS, SUCH AS HEARING LOSS. STRUCTURAL DISORDERS SUCH AS SPINAL CORD INJURY. FUNCTIONAL DISORDERS SUCH AS EPILEPSY, DIZZINESS, NEURALGIA. CANCERS OF THE BRAIN THAT AFFECT THE BRAIN AND THE CENTRAL NERVOUS SYSTEM. AND WE HAVE ACTUALLY A WHOLE LIST OF THE BRAIN AND CNS RECORDED IN THE GMS THAT WE HAVE FOLLOWED OVER THE YEARS. BUT, AGAIN, BY NO MEANS WE CAN SAY THAT EVERYTHING ON THIS LIST IS INCLUDED IN OUR GRANTS, AND WE WELCOME INPUT FROM OTHERS IF WE ARE MISSING ANY.

SO THE CURRENT TRANSLATION AND CLINICAL PORTFOLIO, WHICH IS PRESENTED ON THIS SLIDE, INCLUDES THE PRE-IND MEETING PREPARATION, WHICH IS IN THE TRAN STAGE; IND-ENABLING, WHICH IS OUR CLIN1, AND EARLY CLINICAL; AND THEN MID AND PIVOTAL-LATE CLINICAL.

WHAT I'D LIKE TO ACCENTUATE HERE IS THAT NEURO REPRESENTS 35 PERCENT OF OUR PORTFOLIO IN ALL THESE AREAS, WHICH IS QUITE A SUBSTANTIAL NUMBER.

SO I'M GOING TO RUN BY YOU ALSO ON THE TRAN AND CLINICAL STAGE AWARDS IN NEUROLOGY IN A LITTLE MORE DETAILS PER THIS PIE CHART. WE START

OUT WITH BRAIN CANCER, WHICH COVERS VARIOUS GLIOMAS, INCLUDING GLIOBLASTOMA AND BREAST CANCER BRAIN METASTASES. THEN OCULAR DISEASE, RETINITIS PIGMENTOSA AND AGED-RELATED MACULAR DEGENERATION. THEN WE HAVE ALS. AND YOU CAN TELL BY EACH OF THE CATEGORIES, WE PUT THE NUMBER OF GRANTS THAT ARE IN THAT AREA. FOR EXAMPLE, I WAS SAYING IN BRAIN CANCER, WE HAVE 15 OF THEM. IN OCULAR DISEASE WE HAVE 14. ALS WE HAVE SEVEN. PARKINSON'S DISEASE WE HAVE SEVEN GRANTS. AND ALZHEIMER'S DISEASE WE HAVE SIX. MONOGENIC DISEASES WE HAVE SIX, INCLUDING TAY-SACHS DISEASE, CANAVAN'S DISEASE, FRIEDREICH'S ATAXIA, AND PITT-HOPKINS DISEASE. HUNTINGTON'S DISEASE WE HAVE FIVE. AND WE HAVE EPILEPSY TWO. AND THEN IN NEUROTRAUMA WE ACTUALLY HAVE A LARGE NUMBER, 16 OF THEM, INCLUDING STROKE, SPINAL CORD INJURY. AGAIN, AS I POINTED OUT IN THE GLOSSARY OR CLASSIFICATION, TRAUMATIC BRAIN INJURY, NEONATAL BRAIN HYPOXIA, AND SPINA BIFIDA.

THIS SLIDE ALSO CLARIFIES THE GRANTS BASED ON NUMBER OF NEURO AWARDS IN TRAN VERSUS CLIN1 AND CLIN2. AND A TYPICAL IN THE THERAPEUTIC AREA IS THE GRANTS WE RECEIVE ARE DEPENDENT REALLY ON THE ADVANCEMENT OF THE SCIENCE IN THAT AREA. SO IN THE TRAN AREA, WE HAVE HAD OVER 25 GRANTS INCLUDED.

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CLIN1 WE HAVE LESS, AND THEN IN CLIN2, WHICH IS CLINICAL TRIAL STAGE, WE ARE CLOSER TO THE NUMBER THAT WE SEE IN TRAN. AND SOME OF THESE GRANTS, AS I'LL SHOW YOU LATER, HAVE PROGRESSED FROM TRAN TO CLIN1 TO CLIN 2.

SO THE ACTIVE TRAN AND CLIN STAGE AWARDS CURRENTLY IN NEUROLOGY INCLUDE SEVEN IN OCULAR, SIX IN BRAIN CANCER, SIX IN NEUROTRAUMA, TWO IN ALS, TWO PARKINSON'S DISEASE, ONE HUNTINGTON'S DISEASE, AND ONE EPILEPSY. THE TOTAL AWARDS ARE 25. AND, AGAIN, THE PREVIOUS SLIDES I SHOWED THE CLOSED AND ACTIVE. NOW IT'S MAINLY ACTIVE.

ALSO, THE NEUROLOGY AWARDS BY STAGE AND INDICATION ARE SHOWN ON THIS SLIDE. YOU CAN TELL -- SO THE TRAN ARE IN THE ORANGE COLOR, CLIN1 IS IN THE LIGHT BLUE, AND THE CLIN2 IS IN THE DARK BLUE.

WE'RE AIMING TO MOVE AS MANY OF THESE PROGRAMS FROM THE TRAN STAGE, THE TRAN COLOR, TO CLINICAL TRIALS. AND YOU SEE HERE THAT, AGAIN, WE HAVE A SUBSTANTIAL NUMBER THAT ARE BRAIN CANCER, IN OCULAR MORE IN CLIN2 AND TRAN THAN CLIN1, AS I SHOWED YOU BEFORE. INTERESTINGLY ENOUGH, IN ALS WE HAVE MORE IN CLIN2 THAN IN TRAN. HUNTINGTON'S DISEASE, EQUIVALENT, MEANING TRAN, CLIN1, AND CLIN2. THEN WITH ALZHEIMER'S DISEASE, WE MAINLY HAVE TRAN.

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PARKINSON'S WE HAVE EQUAL NUMBER IN CLIN1 AND CLIN2.

I JUST WANTED TO DRAW YOUR ATTENTION TO THE NEUROTRAUMA AREA WHERE WE HAVE A LARGE NUMBER IN TRAN AND A GOOD NUMBER IN CLIN2 AND A SMALLER NUMBER IN CLIN1.

PROCEEDED TO SHARE WITH YOU THE ACTUAL ACTIVE NEUROLOGY TRIALS THAT ARE PHASE 1. AS OUR MISSION SPEAKS TOWARDS ADVANCING PROGRAMS TOWARDS POTENTIAL APPROVAL, IT'S IMPORTANT THAT WE RECOGNIZE HOW MANY OF THOSE PROGRAMS ARE IN PHASE 1 TRIAL AND WHERE THEY'RE HEADING TO PHASE 2 OR 3.

SO THIS SLIDE SHOWS THAT REALLY, AGAIN, WE HAVE 11 OF THOSE PHASE 1 TRIALS IN DIFFERENT DISEASE INDICATIONS RANGING FROM ALS TO, AGAIN, GBM TO PEDIATRIC GLIOMA, STROKE, ET CETERA. AND YOU CAN FOLLOW, SOME OF THOSE PHASE 1 TRIALS ARE AT CEDARS-SINAI WHICH HAS ONE OF OUR NEWEST ALPHA CLINICS, UC DAVIS, CITY OF HOPE WITH AT LEAST THREE OF THEM.

AND THE LAST ONE YOU SEE HERE IS RETINITIS PIGMENTOSA, WHICH IS, AGAIN, BEING CONDUCTED -- THE TRIAL IS BEING DONE ALSO AT CEDARS-SINAI.

THE NEUROLOGY TRIALS IN PHASE 2 AND 3 ARE QUITE SMALL. SO MEANING THERE'S A SMALL NUMBER OF THEM. THERE ARE TWO OPHTHALMOLOGY ONES, AND BOTH OF

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THEM ARE COMPLETED AND CLOSED. AND THEN THERE'S ONE IN PHASE 3, WHICH WAS ALSO COMPLETED AND CLOSED. THEY WERE ALL RUN AT UCI AS THE ALPHA CLINIC.

WHAT WE WANTED TO GET YOU TO SEE IS THE FACT THAT MANY OF OUR GRANTS ACTUALLY START OUT IN DISC, GO TO TRAN, THEN TO CLIN1, THEN TO CLIN2. AND THIS IS A TRIBUTE TO THE FACT THAT THESE SCIENTISTS AND CLINICIANS CONTINUE TO ADVANCE THEIR PROGRAMS WITH OUR DOLLARS AND ENTHUSIASM FOR KEEPING THESE PROGRAMS GOING.

SO WE HAVE HERE A TON OF THEM THAT ARE MOVING FROM DISC TO CLIN2 OR HAVE MOVED TO CLIN2. SOME MAY HAVE HAD ALREADY, LIKE DR. KLASSEN HAS HAD TWO CLIN2S ALREADY IN FOR THE SAME INDICATION.

SO THIS CONCLUDES WHAT THE CIRM PORTFOLIO LOOKS LIKE, BUT I WANTED TO SHOW YOU THE APPROVED NEUROLOGY CELL AND GENE THERAPIES PER THE OUTLINE I DESCRIBED EARLIER. THERE ARE DRUGS THAT ARE ON THE MARKET ALREADY FOR LUXTURNA FOR LEBER CONGENITAL AMAUROSIS, WHICH IS A RETINAL DISEASE, THAT WAS APPROVED IN 2017. ACTUALLY SPARK THERAPEUTICS LED THE WHOLE AREA OF LEBER CONGENITAL AMAUROSIS, WHICH IS A FORM OF RETINITIS PIGMENTOSA. AND IT HAS UNIQUE FEATURES IN THE SENSE THEY GOT THE DRUG APPROVED BASED ON THE PATIENT'S NEED FOR EYESIGHT IN

THE DARK. AND THEY WERE THEN ABLE TO MANEUVER A MOBILITY TEST IN ORDER TO ADVANCE THE PROGRAM FORWARD TO APPROVAL. AND THAT WAS THE KEY ENDPOINT THAT WAS USED IN GETTING THAT PROGRAM APPROVED.

SO ZOLGENSMA IS FOR SMA, WHICH IS SPINAL MUSCULAR ATROPHY. IT WAS APPROVED IN 2019. AND I'M SURE YOU'VE OFTEN SEEN PHOTOS OF THE LITTLE GIRL RUNNING AROUND WHO'S BEEN TREATED WITH THIS GENE THERAPY MODALITY AND HAS DONE VERY WELL AS A POSTER CHILD OF THAT EFFORT.

THEN WE HAVE LIBMELDY, WHICH IS AN EX VIVO HASPC GENE THERAPY FOR METACHROMATIC LEUKODYSTROPHY, AND THAT WAS APPROVED IN 2020. IT WAS APPROVED IN THE EU, BUT U.S. FILING IS PLANNED FOR THIS YEAR.

UPSTAZA FOR AROMATIC L-AMINO ACID DECARBOXYLASE DEFICIENCY, WHICH WAS APPROVED IN 2022. THERE'S A COUPLE MORE THAT I JUST READ ABOUT, BUT THIS GIVES YOU A FEELING FOR THE FIELD IS ADVANCING AND ADVANCING WELL WITH A NUMBER OF INDICATIONS. BUT SOME OF THESE, IF NOT MOST OF THESE, ARE RARE DISEASE INDICATIONS. THAT'S IMPORTANT TO HIGHLIGHT BECAUSE RARE DISEASES ARE LEADING THE WAY AS EITHER MONOGENIC DISEASES AND POSTER CHILDS FOR GENE THERAPY MODALITIES. SO IT'S EASIER TO IDENTIFY WHETHER THE TRIAL ACTUALLY WAS

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SUCCESSFUL OR NOT BASED ON THE OUTCOME OF THE STUDY AND THE ENDPOINTS THAT ARE USED. AND THEY HAVE A RELATIVELY SMALL NUMBER OF PATIENTS. AND ALSO FDA HAS BEEN ADVANCING MANY OF THOSE PROGRAMS MUCH MORE EASILY USING THE ACCELERATED APPROVAL PATHWAY, ESPECIALLY IF THEY HAVE ANY KIND OF A BIOMARKER.

THERE ARE FIVE PENDING FDA DECISIONS IN NEUROLOGY FOR 2023. THE ONE THAT I HIGHLIGHTED IS THE FRIEDRICH ATAXIA, WHICH IS THE FIRST TREATMENT FOR FRIEDRICH ATAXIA, WHICH IS, AGAIN, A RARE DEGENERATIVE NEUROMUSCULAR DISORDER. THE RETT SYNDROME DRUG FOR, AGAIN, A RARE GENETIC DISORDER OF BRAIN DEVELOPMENT. THEN THE SOD1 ALS FOR BIOGEN, WHICH IS FIRST TARGETED FOR THERAPY FOR SOD1 MEDIATED ALS. THEN PARKINSON'S DISEASE WITH AMNEAL PHARMACEUTICALS. AGAIN, THE FEATURE THAT'S VERY EXCITING ABOUT THIS DRUG IS THE CARBIDOPA/LEVODOPA COMBINATION, WHICH IS THE FORMULATION THAT MADE THIS DRUG POSSIBLE, WHICH IS AN EXTENDED RELEASE CAPSULE. SO THE DELIVERY MECHANISM, THE FORMULATION MADE THE DRUG A SUCCESS.

AND THEN THE CERVICAL DYSTONIA, WHICH IS NOVEL BOTULINUM TOXIN TYPE A FORMULATION. THIS IS, AGAIN, FOR CERVICAL DYSTONIA WITH A PDUFA DATE OF AUGUST 19, 2023. AND THIS SPEAKS TO A THEME THAT

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LARRY HAS TALKED TO US ABOUT IN THE PAST, WHICH IS REPURPOSING DRUGS IN ORDER TO ACHIEVE A NEW INDICATION AND SUCCESS FOR TREATING PATIENTS WHO HAVE UNMET MEDICAL NEED.

I'M NOT GOING TO GO OVER THIS LAST SLIDE, BUT I WANT TO CUE YOU TO BE AWARE THAT PER *NATURE* ARTICLE, THERE ARE 11 CLINICAL TRIALS THAT WILL SHAPE MEDICINE IN 2023 AND MAINLY HIGHLIGHT TWO OF THEM. PARKINSON'S DISEASE, POTENTIAL APPROVAL FOR A DRUG CALLED EXENATIDE. AND THIS IS EXCITING IF IT GETS APPROVED. AND THEN ALSO EISAI/BIOGEN ANTIBODY FOR ALZHEIMER'S DISEASE. AND THERE IT'S ON THE ACCELERATED APPROVAL PATH.

AND SO WITH THAT, I THINK I WILL CONCLUDE BY OUR KEY FINDINGS, MEANING THAT, AGAIN TO REITERATE, NEURO COMPOSES ABOUT 35 PERCENT OF THE TRANSLATION AND CLINICAL PORTFOLIO. ALL ACTIVE NEURO TRIALS, 11 OUT OF 11, ARE IN PHASE 1 EARLY CLINICAL DEVELOPMENT. SEVERAL ARE IN RARE DISEASES, AND THAT'S CONSISTENT WITH MY EARLIER STATEMENT AND CONSISTENT WITH THE FIELD. WITH THAT, I'LL STOP AND HAPPY TO ENTERTAIN ANY QUESTIONS.

CHAIRMAN GOLDSTEIN: SO THANK YOU VERY MUCH, ABLA. THAT'S EXTREMELY INFORMATIVE.

BEFORE WE OPEN IT UP GENERALLY, I JUST

WANT TO KICK OFF THE QUESTIONS WITH SO I KNOW THAT YOU ARE, AND PERHAPS OTHER CIRM TEAM MEMBERS, PURSUING WHAT'S SOMETIMES CALLED A HUNTING STRATEGY. COULD YOU JUST EXPLAIN THAT BRIEFLY?

DR. CREASEY: OF COURSE. SO ACTUALLY WE CREATED SLIDES. TOO BAD I DON'T HAVE THEM READY HERE. LET ME EXPLAIN TO YOU WHAT HUNTING MEANS. HUNTING MEANS THAT -- IS ACTUALLY COMPOSED OF SEVERAL FEATURES. ONE IS WE READ THE LITERATURE. WE ATTEND MEETINGS. PEOPLE APPROACH US. WE DISCUSS AMONGST OURSELVES, MEANING THE WHOLE CIRM TEAM, WHO TO TALK TO AND HOW TO APPROACH THEM. WE ACTUALLY ALSO GO AFTER WHERE WE THINK THERE'S AN UNMET MEDICAL NEED THAT WE HAVE NOT BEEN APPROACHED BY. AND SO WE CONTACT CLINICIANS, ACADEMICIANS, PHYSICIAN SCIENTISTS AND INVITE THEM TO APPLY.

SO IT IS NOT A -- HUNTING IS THE OPPOSITE OF PASSIVE. WE ACTUALLY GO AFTER IT IN MULTIPLE WAYS, AGAIN, WITH KEEPING IN MIND THE NEED FOR ADVANCING OUR PORTFOLIO AND KEEPING US IN THE KNOW REGARDING ALL THE NEW SCIENCE, WHETHER IT'S TECHNOLOGY OR AREAS OF UNMET MEDICAL NEED.

TECHNOLOGIES OFTEN EXCITE US. AND SO, FOR EXAMPLE, THE UNMET NEED, DURING THE COVID PANDEMIC, WE HAD SOME APPROACH US FOR POTENTIAL GRANTS, AND WE

ALSO APPROACHED OTHERS FOR POTENTIAL GRANTS. AND SO THAT'S HOW WE ENDED UP WITH A COVID PORTFOLIO. AND SO THAT'S JUST ONE SIMPLE EXAMPLE.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU, ABLA.

THE REASON I WANTED TO JUST HIGHLIGHT THAT IS, TO THE BEST OF CIRM'S ABILITY AND PERHAPS OUR ABILITY AS A BOARD, WE DON'T THINK THAT THERE ARE GREAT PROJECTS HIDING AROUND CALIFORNIA THAT WE DON'T KNOW ABOUT AND THAT SHOULD BE FUNDED. IT'S ALWAYS POSSIBLE, OF COURSE, BUT I THINK THE CIRM TEAM HAS REALLY DONE A GOOD JOB TRYING TO ROOT THOSE OUT AND WORK WITH THEM.

SO LET ME OPEN IT UP TO QUESTIONS FROM THE GROUP BEFORE WE GO TO SHYAM. PLEASE RAISE YOUR HAND. J.T., GO AHEAD.

DR. THOMAS: SO, ABLA, JUST TO FOLLOW UP ON LARRY'S QUESTION. I HAD MENTIONED AN UPDATE FOR THE BOARD ON THE HUNTING PROCESS, AND I THINK THAT'S GOING TO BE ON THE MARCH AGENDA; IS THAT CORRECT?

DR. CREASEY: YES. YES. WE ACTUALLY ARE PREPARING SLIDES.

DR. THOMAS: GREAT. THANK YOU.

MY SECOND QUESTION IS, AND YOU MAY HAVE MENTIONED THIS AND I COULD HAVE MISSED IT IN YOUR

PRESENTATION. THANK YOU FOR THAT PRESENTATION, BY THE WAY. VERY HELPFUL. THERE WAS THE ONE SLIDE THAT HAD PROGRESSION EVENTS SHOWING EARLY FUNDING THAT'S PROGRESSED TO CLIN1 OR CLIN2. HAVE WE HAD EARLY FUNDING THAT WE DIDN'T SEE PROGRESS, BUT OTHERS HAVE FUNDED SUBSEQUENTLY IN LATER STAGES OF RESEARCH?

DR. CREASEY: THE SIMPLE ANSWER IS YES. SOME HAVE ELECTED NOT TO COME BACK TO US. SOME, LIKE, APPLIED TO NIH OR OTHER NONPROFIT ORGANIZATIONS, ET CETERA. BUT WE HAVE HAD SOME THAT WENT AWAY AND CAME BACK. WE HAVE NOT CAPTURED THIS IN THE PROGRESSION EVENTS SLIDE.

DR. THOMAS: IS THERE ANY WAY TO -- THERE MAY BE SOME THAT WE FUNDED EARLY AND WENT AWAY AND HAVE NOT COME BACK, WHICH I THINK YOU ALLUDED TO. IS THERE ANY WAY TO GET SORT OF UPDATED DATA ON THOSE?

DR. CREASEY: SURE. NO PROBLEM.

DR. THOMAS: THANK YOU.

CHAIRMAN GOLDSTEIN: MARV.

DR. SOUTHARD: SO I WAS WONDERING IF THERE MIGHT BE SOME KIND OF PREHUNTING ACTIVITY BECAUSE AS A MENTAL HEALTH AND ADDICTION SPECIALIST ADVOCATE, IT DOESN'T LOOK LIKE THERE ARE ANY PARTICULAR

PROJECTS IN THE SCHIZOPHRENIA, BIPOLAR DISORDER, ADDICTION AREA AT ALL. AND IF YOU'RE ALREADY LOOKING AT POSSIBLE THINGS THAT ARE IN DEVELOPMENT, MAYBE THERE'S SOMETHING WE NEED TO DO TO SEED DEVELOPMENT.

DR. CREASEY: THANK YOU, MARV, FOR THE QUESTION. I JUST WOULD LIKE TO HIGHLIGHT THAT ONE OF OUR REQUIREMENTS, FOR THE PROJECTS THAT APPLY, THERE'S AN INVOLVEMENT WITH STEM CELLS IF IT IS A SMALL MOLECULE OR A LARGE MOLECULE. AND ALSO THEN IF IT WERE A GENE THERAPY FOR A KNOWN, LIKE IF THERE'S ONE SINGLE GENE INVOLVED, LET'S SAY, FOR AUTISM, THEY COULD EASILY HAVE APPLIED OR WE WOULD HAVE GONE AFTER THEM. SO IT'S A COMBINATION OF WHAT WE CONSIDER ELIGIBLE AND ALSO WHETHER THE CLINICAL TRIALS ARE AMENABLE TO OR THE RESEARCH IS AMENABLE TOWARDS GENE THERAPY OR AN RNA THERAPY, ET CETERA.

DR. SOUTHARD: OBVIOUSLY WHATEVER WE'RE GOING TO BE DOING IS GOING TO BE DOING SOMETHING WITH SOME STEM CELLS. BUT, FOR EXAMPLE, IF YOU GOOGLE STEM CELL TREATMENT FOR ADDICTION AND YOU LOOKED AT WHAT COMES UP, THERE'S NOT MUCH, BUT WHAT DOES COME UP IS SOMETHING THAT SAYS THERE ARE PROJECTS UNDER DEVELOPMENT, BUT THEY ARE PROBABLY NOT GOING TO REACH ANY FULFILLMENT FOR FIVE TO TEN

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YEARS. SO GET INTO RECOVERY NOW. IT WAS FROM A RECOVERY PLACE.

SO OBVIOUSLY I DON'T KNOW AS MUCH YOU ALL DO ON THESE THINGS, BUT IT SEEMS TO ME THAT IF WE ARE LOOKING, IF WE ARE WANTING THINGS IN SCHIZOPHRENIA, BIPOLAR DISORDER, AND ADDICTION, WHICH I THINK WE ARE, HOW DO WE BEGIN TO APPROACH THAT, I GUESS, IS MY QUESTION.

DR. CREASEY: VERY IMPORTANT QUESTION. AND WE ACTUALLY ARE DISCUSSING IT OURSELVES, AND WE'D LOVE GUIDANCE FROM YOU GUYS AND GALS. WHAT'S IMPORTANT HERE, THOUGH, IS TO POINT OUT, AND I'M SPEAKING NOW OUT OF I DO NOT RUN THE DISCOVERY PROGRAM. MY COLLEAGUE ROSA DOES. AND MY RECOLLECTION IS WE HAVE SEVERAL, FOR EXAMPLE, PROGRAMS IN DISCOVERY THAT ADDRESS, LIKE, AUTISM. AND SO WE ARE STARTING -- WE HAVE BEEN GATHERING SOME OF THOSE, BUT NOT NECESSARILY ANY OF THEM HAVE MOVED ON OUR OWN WATCH TOWARDS TRANSLATION AND CLINICAL YET.

CHAIRMAN GOLDSTEIN: MARV, I'LL JUST NOTE THAT THIS HAS BEEN A TOPIC THAT THERE'S BEEN QUITE A BIT OF DISCUSSION ABOUT BETWEEN ME AND MEMBERS OF THE CIRM TEAM AND FOLKS ON THE OUTSIDE. AND WE WILL ABSOLUTELY BE RETURNING TO THIS ISSUE BECAUSE IT'S

AN IMPORTANT ONE.

OKAY. FRED, YOU'RE UP.

DR. FISHER: THANKS SO MUCH. I THINK THE PRESENTATION HELPS GIVE US A REALLY GOOD BASELINE IN TERMS OF WHERE WE ARE TODAY AND WILL INFORM CONVERSATIONS ABOUT WHERE WE ARE GOING.

QUICK QUESTION. I APOLOGIZE IN ADVANCE IF I MISSED IT. IS MS, I DON'T RECALL HEARING IT OR SEEING IT ON THE LIST. AGAIN, APOLOGIES IF I MISSED IT. IS MS PART OF THIS?

DR. CREASEY: WE HAVE NOT HAD ANY MS GRANTS IN TRAN AND CLINICAL.

DR. FISHER: BUT IT IS -- MS GRANTS THAT ARE GENE OR STEM CELL THERAPY FOCUSED WOULD BE CONSIDERED NEURO GRANTS?

DR. CANET-AVILES: YES, OF COURSE.

DR. MILLAN: AND THEY'RE ELIGIBLE.

DR. FISHER: GREAT. THANKS. I JUST DIDN'T SEE IT LISTED SPECIFICALLY ANYWHERE AND WANTED TO BE CLEAR ONE WAY OR ANOTHER.

DR. CREASEY: AGAIN, FRED, WHAT'S IMPORTANT, WHAT I SAID IS THAT OUR GLOSSARY IS MAYBE INCOMPLETE. AND WE WILL ADD TO IT AS WE ARE PROGRESSING WITH THE TASK FORCE.

DR. CANET-AVILES: JUST TO ADD, IN

DISCOVERY WE HAVE FIVE AWARDS THAT HAVE BEEN IN PORTFOLIO, BUT WE DON'T CURRENTLY HAVE ANY. SO WE WILL GO INTO THIS PART OF THE PORTFOLIO AT ANOTHER TIME WHEN DR. GOLDSTEIN MENTIONS IT.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU. MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: THANK YOU. CAN YOU SPEAK TO THE HUNTING A LITTLE MORE? I KNOW YOU ARE GOING TO GIVE A PRESENTATION AT THE BOARD, BUT I THINK IT'S IMPORTANT IN THIS CONTEXT TO TALK ABOUT HOW THE PROJECTS HAVE BEEN COMING. AND JUST TO CLARIFY, TO DATE THERE HAS NOT BEEN A DIRECTIVE TO THE TEAM TO LOOK STRICTLY FOR NEURO PROJECTS, CORRECT? IT HAS JUST BEEN THE PROMISING PROJECTS IN CALIFORNIA AND HOW DO WE BRING THEM INTO THE FOLD VERSUS A GROUP LIKE THIS WHERE THE BOARD COULD DIRECT YOU AND THE TEAM TO GO SPECIFICALLY FOR NEURO, SOME SORT OF NEURO, WHETHER IT'S NEUROPSYCHE OR NEURODEGENERATIVE, IF THAT WERE THE DIRECTION MOVING FORWARD.

DR. CREASEY: THANK YOU, MARIA. THE INSTRUCTIONS FOR TRAN AND CLIN TEAMS ARE TO GO AFTER NEURO INDICATIONS FOR THE PAST AT LEAST YEAR WHERE WE MADE THAT THE HIGHEST PRIORITY IN IDENTIFYING NEURO PROGRAMS WITHIN THE STATE AND OUTSIDE THE

STATE THAT WOULD COME APPLY. AND SO THAT'S ALREADY ON OUR RADAR.

WE, IN FACT, THE TEAM, WE MEET FOR OUR HUNTING. WE PRIORITIZE NEURO AS THE FIRST TOUCHPOINTS WE'VE MADE IN NEURO PROGRAMS. AND WE DISCUSS HOW BEST TO APPROACH ONE COMPANY VERSUS ANOTHER OR ACADEMIC INSTITUTION VERSUS ANOTHER. SO I THINK THAT PRIORITIZATION OF NEURO IS ON OUR MIND. IN FACT, IT'S BEEN ON OUR MIND SINCE THE PROPOSITION PASSED. IT'S A MATTER OF THE AVAILABILITY OF INVESTIGATORS IN THE STATE THAT ARE WILLING TO APPLY.

CHAIRMAN GOLDSTEIN: THANK YOU. PAT.

DR. LEVITT: THANKS VERY MUCH. THAT WAS GREAT. THE PROPOSITION IS -- CONTEXT FOR THE PROPOSITION AND THE MANDATE IS THE CONTEXT IS DOLLARS. AND SO I'M WONDERING -- I HAVE A MUCH BETTER SENSE NOW OF THE NUMBER OF PROJECTS, THE KIND OF PROJECTS, THE PERCENTAGE ON THAT PIE CHART. WHERE DO THOSE PROJECTS SIT IN TERMS OF THE FRACTION OF THE 1.5 BILLION THAT IS LISTED SPECIFICALLY IN THE PROPOSITION, WHICH WOULD GIVE US AN ADDITIONAL INFORMATION ABOUT, NOT JUST THE SCIENTIFIC GAPS THAT PEOPLE HAVE BEEN BRINGING UP, BUT ALSO THE FINANCIAL GAPS AND CHALLENGES?

DR. CREASEY: I THINK DR. GOLDSTEIN RECEIVED THAT ANSWER JUST A FEW MINUTES AGO. YOU WANT TO PROVIDE IT?

CHAIRMAN GOLDSTEIN: ARE YOU REFERRING TO THE TABULATION FOR DISC DOLLARS THAT YOU GAVE ME, OR DID THAT INCLUDE NEURO -- SORRY.

DR. CREASEY: I CAN SAY I THINK IT'S 30 PERCENT OF THE R&D BUDGET HAS BEEN SPENT ON NEURO, PROPOSITION 14 R&D BUDGET.

UNIDENTIFIED SPEAKER: IT'S $129 MILLION.

DR. CREASEY: THE ACTUAL NUMBER IS 129 MILLION.

DR. LEVITT: SO 129 MILLION, 30 PERCENT HAS BEEN SPENT SO FAR ON R&D OUT OF THE MANDATE FOR 1.5 BILLION, RIGHT?

DR. CANET-AVILES: CORRECT.

DR. LEVITT: THANK YOU.

SO I DON'T KNOW THE DETAILS OF THIS. THERE'S CLEARLY A LOT OF IPS CELL WORK AND ORGANOID WORK, ET CETERA -- WE HAD A MEETING LIKE MAYBE IT WAS OVER A YEAR AGO. I CAN'T REMEMBER ANYMORE -- WHERE A NUMBER OF SCIENTISTS IN CALIFORNIA WHO TALKED ABOUT THAT KIND OF WORK. I ASSUME -- I KNOW THAT THAT'S ON YOUR RADAR, BUT IS ANY OF THAT WORK IN THAT PORTFOLIO IN THE DISC PORTFOLIO OR THE

TRANSLATIONAL PORTFOLIO?

DR. CANET-AVILES: IT IS. THE IPS WORK WOULD BE CONSIDERED PART OF THE EARLIER PART OF OUR PORTFOLIO, AND WE WILL BE BEGINNING TO GET MORE GRANULARITY IN THE FUTURE ABOUT THIS DEFINITELY.

DR. LEVITT: AND THEN MAYBE ONE OTHER JUST -- SORRY, LARRY. ONE OTHER, I DON'T KNOW THE DETAILS OF THIS. HOW DO RESEARCH INVESTIGATORS OUTSIDE OF THE STATE OF CALIFORNIA THAT KNOW THEY'RE DOING WORK THAT'S ELIGIBLE FOR CIRM FUNDING, HOW DO THEY FIND OUT ABOUT THAT? OR HOW ARE YOU ALL THINKING ABOUT THE BEST WAY OF -- I UNDERSTAND THE HUNT COMPONENT, WHICH CAN BE VERY SUCCESSFUL, BUT HOW DO RESEARCHERS OR INVESTIGATORS IN GENERAL FIND OUT, IF THEY'RE OUTSIDE OF THE STATE OF CALIFORNIA, ABOUT THEIR ELIGIBILITY TO BE ABLE TO APPLY FOR CIRM FUNDING?

DR. CREASEY: ALL SCIENTISTS AT CIRM ARE EQUIPPED WITH ELIGIBILITY CRITERIA. AND IN COLLABORATION WITH BUSINESS DEVELOPMENT, WE REACH OUT TO PEOPLE OUTSIDE THE STATE. AND, IN FACT, AS PER OUR MISSION, WE CAN FUND GLOBALLY. IN FACT, ONE OF OUR GRANTS CAME FROM -- THE GRANTEE WAS FROM ISRAEL. AND SO WE CONSTANTLY REACH OUT TO SCIENTISTS AND CLINICIANS THROUGHOUT THE COUNTRY WHO

HAVE EITHER PUBLISHED A RECENT PAPER OR WE HAPPEN TO MEET THEM AT A CONFERENCE, AND WE SHARE WITH THEM THE ELIGIBILITY CRITERIA. WHEN IT COMES TO DISC AND TRAN, ONLY CITIZENS OF CALIFORNIA CAN APPLY. BUT WHEN IT COMES TO CLIN1 AND CLIN2, THOSE CAN BE -- APPLICANTS FROM OUTSIDE THE STATE CAN APPLY.

SO THAT'S WHAT WE TALK ABOUT. CLIN1, WHICH IS IND-ENABLING STUDIES, AND THEN CLIN2, WHICH IS CONDUCTING THE TRIAL, WE FUND FOR OUTSIDE THE STATE OF CALIFORNIA.

DR. LEVITT: SO ARE ANNOUNCEMENTS SENT TO, FOR EXAMPLE, UNIVERSITIES, DIRECTORS OF RESEARCH OR FREESTANDING RESEARCH INSTITUTES? DO THEY RECEIVE THEM AND THEN ARE ABLE TO DISTRIBUTE THEM? I KNOW THE INDIVIDUAL INVESTIGATOR CONTACT IS HELPFUL, AND THAT'S PART OF THE HUNTING PROCESS, BUT FOR BROADER DISTRIBUTION WITH THE ELIGIBILITY CRITERIA NOTED. I DON'T KNOW IF YOU REGULARLY DO THAT. SO THERE'S VICE PRESIDENTS FOR RESEARCH AT UNIVERSITIES, ET CETERA, OUTSIDE OF CALIFORNIA OR WORLDWIDE BASED ON THE TYPES OF GRANTS.

DR. CREASEY: THANK YOU FOR BRINGING THAT UP. WE ACTUALLY HAVE RECENTLY STARTED SOMETHING LIKE THAT. IN FACT, ONE OF OUR RECENT RECRUITS RECOMMENDED WHY NOT CREATE EVEN PAMPHLETS THAT GO

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WITH THE LETTERS THAT THEY CAN PUT ON THEIR BULLETIN BOARDS AND HAVE THEM SHARED WITH THEIR FACULTY MEMBERS.

DR. LEVITT: YEAH. THERE ARE PEOPLE ON THIS CALL HAVE THAT. WHEN I RECEIVE SOMETHING IN MY OFFICE AS CHIEF SCIENTIFIC OFFICER, I HAVE AN ELECTRONIC BULLETIN BOARD. I DON'T KNOW IF WE HAVE ANY BULLETIN BOARDS ANYMORE. BUT THAT BEING SAID, THEN THE DISTRIBUTION IS TO SEVERAL HUNDRED INVESTIGATORS. I THINK THAT WILL HELP BECAUSE WE HAVE -- THE PORTFOLIO IS IMPRESSIVE MORE THAN I HAD THOUGHT, BUT WE'RE GOING TO NEED A WIDER REACH, PARTICULARLY IN AREAS IN WHICH WE HAVE LITTLE TO NO ACTIVITY. AND THAT HAS ALREADY BEEN MENTIONED. THANK YOU, LARRY. THANKS VERY MUCH.

DR. CREASEY: WE HAVE NO SHORTAGE OF GRANTS BEING SUBMITTED. WE HAVE, IN GENERAL, FOR CLIN1 AND CLIN2, WE GET NOW SEVERAL A MONTH SINCE WE HAVE THE 12 MONTHS A YEAR THAT THEY CAN APPLY. AND WHAT IS INTERESTING IS THAT WE NEED TO MAYBE -- THE CLIN2 EITHER THROUGH OUR HUNTING OR PASSIVELY. AND SO IF WE WANT TO HAVE DIFFERENT TYPE OF APPLICANTS, THEN MAYBE THAT WOULD BE A DIFFERENT DISCUSSION AT SOME POINT WITH THE TASK FORCE.

CHAIRMAN GOLDSTEIN: ABLA, I HAVE TO

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CONFESS I'M A LITTLE CONFUSED. I THOUGHT THAT THE PROPOSITION LIMITED FUNDING TO PROJECTS IN CALIFORNIA EXCLUSIVELY WITH A LOOPHOLE FOR COLLABORATIONS. WHAT AM I MISSING HERE?

DR. CREASEY: FOR CLIN1 AND CLIN2, WE FUND OUTSIDE THE STATE. AM I RIGHT? YES. OUTSIDE THE STATE OF CALIFORNIA.

DR. CANET-AVILES: IT'S FOR EVERYTHING MINUS CLIN1, CLIN2.

DR. MILLAN: PROVIDED THAT THE FUNDS ARE EXPENDED IN CALIFORNIA.

CHAIRMAN GOLDSTEIN: THERE WE GO. OKAY. SO THE DOLLARS HAVE TO STAY IN CALIFORNIA FOR PROJECTS THAT HAVE A PI OUTSIDE OF CALIFORNIA; IS THAT CORRECT?

DR. CREASEY: FUNDS HAVE TO BE EXPENDED IN CALIFORNIA BASED ON THE ACTIVITIES THEY DO IN CALIFORNIA. FOR EXAMPLE, THEY CAN MANUFACTURE IN CALIFORNIA. THEY CAN DO THEIR TOXICOLOGY STUDY IN CALIFORNIA. AND THAT'S WHAT WE REQUIRE FOR THE IND-ENABLING STUDIES. BUT FOR CLINICAL, THEY HAVE TO HAVE A PI IN CALIFORNIA WITH A CLINICAL SITE THAT ARE GOING TO ENROLL PATIENTS FOR THE CLINICAL TRIALS EVEN THOUGH THE APPLICANT, LET'S SAY, IS FROM NEW YORK.

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CHAIRMAN GOLDSTEIN: OKAY. SO IT'S NOT EVERYWHERE IN THE WORLD EASILY WE CAN FUND. THERE REALLY HAS TO BE A CENTER OF ACTIVITY IN CALIFORNIA TO BE ELIGIBLE.

DR. CREASEY: CORRECT. CORRECT.

CHAIRMAN GOLDSTEIN: GREAT. MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: COUPLE QUICK QUESTIONS FOR HISTORICAL REFERENCE. HAVE WE EVER DONE REQUESTS FOR PROPOSALS AND/OR ENSORTIA MEETING AROUND SPECIFIC TOPICS RELATED TO LOOK AT HUNTING FOR ELEMENTS IN A DIFFERENT WAY? JUST CURIOUS ABOUT THOSE TWO MODALITIES.

DR. CREASEY: I'VE BEEN HERE SINCE 2016, MEANING AT CIRM. WE HAVE NOT DONE THAT. WE'VE TALKED ABOUT IT AT LEAST A COUPLE OF TIMES. MARIA, YOU WANT TO SAY. HAVE WE DONE IT?

DR. MILLAN: TO THE BEST OF MY KNOWLEDGE, AND I THINK GIL SAMBRANO WHO WOULD HAVE PROBABLY BEEN HERE, J.T., WE HAVEN'T HAD A THEME-SPECIFIC CALL, LIKE A MOONSHOT OR THEMATIC, BUT THAT IS SOMETHING THAT IS IN THE STRATEGIC PLAN AS AN AREA THAT WE CAN GO TOWARD TO HAVE A CONSORTIUM APPROACH, BUT WE HAVE NOT YET DONE THAT TO DATE.

DR. THOMAS: TO MY KNOWLEDGE, I AGREE WITH

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THAT STATEMENT.

DR. FISCHER-COLBRIE: GREAT. THANK YOU.

CHAIRMAN GOLDSTEIN: THANK YOU, MARK. J.T.

DR. THOMAS: ABLA, ONE OTHER HUNTING RELATED QUESTION. A TYPICAL FACT PATTERN WOULD BE A COMPANY OUTSIDE OF CALIFORNIA WANTS TO HAVE ONE OF ITS TRIAL SITES IN CALIFORNIA AND APPLIES WITH RESPECT TO THE COST ATTACHED TO THAT. DO YOU KNOW IF THE ACADEMIC INSTITUTIONS HUNT THEMSELVES? DO THEY GO OUT TRYING TO SOLICIT COMPANIES FROM OUTSIDE OF CALIFORNIA TO COME TO CALIFORNIA TO DO PART OF THEIR CLINICAL TRIALS HERE SUCH THAT -- AND USE AS POTENTIAL BAIT FOR THAT, IF YOU WILL, THAT THERE'S THE POSSIBILITY OF APPLYING FOR CIRM FUNDING FOR THAT COMPONENT? DO WE KNOW IF THAT SORT OF THING HAPPENS?

DR. CREASEY: I THINK IT HAPPENS FREQUENTLY ACTUALLY. IT'S A WAY TO ENHANCE COLLABORATION. AND I CAN THINK OF AT LEAST A COUPLE OF EXAMPLES THAT THAT'S THE CASE. FOR EXAMPLE, I DON'T WANT TO SPEAK ABOUT THE PROJECTS, BUT AT LEAST I CAN CITE A COUPLE AT SOME POINT, YEAH.

DR. MILLAN: AND THE OTHER PART OF THAT IS TRUE AS WELL, J.T. MANY INDUSTRY PARTNERS ARE

ACADEMIC INVESTIGATORS WHO ARE VERY INTERESTED IN BEING ABLE TO COLLABORATE WITH CALIFORNIA INVESTIGATORS OR MOTIVATED TO DO SO BECAUSE OF THE POTENTIAL FUNDING OF THAT COLLABORATION.

DR. THOMAS: SURE, ABSOLUTELY. I WAS JUST CURIOUS ABOUT THE OPPOSITE. YEAH BECAUSE THAT'S -- I WOULD THINK THAT WOULD BE A GOOD RECRUITING TOOL TO GET COMPANIES TO COME TO CALIFORNIA WITH RESPECT TO PARTICULAR SITES OR WHATEVER FOR THE INSTITUTIONS IN QUESTION.

DR. LEVITT: J.T., THERE'S A DATA PLATFORM, TRINETX -- SOME PEOPLE MAY BE FAMILIAR WITH THAT -- WHERE ELECTRONIC HEALTH RECORDS THAT ARE DEIDENTIFIED AT INSTITUTIONS ARE AVAILABLE FOR COMPANIES TO SEARCH THROUGH. WE GET CONTACTED ALL THE TIME, THAT THEY CAN SEE HOW MANY PATIENTS ARE AT CHLA WITH A CERTAIN IDC CODE. THESE ARE PHARM AND BIOTECH COMPANIES THAT ARE INTERESTED IN DOING CLINICAL TRIALS. AND THEY'RE INTERESTED TO FIGURE OUT WHETHER THEY WANT TO DO IT AT YOUR PARTICULAR SITE. I'M SURE THERE ARE OTHER INSTITUTIONS IN CALIFORNIA, I KNOW THERE ARE OTHER INSTITUTIONS IN CALIFORNIA THAT HAVE THE SAME THING. THEIR ELECTRONIC HEALTH RECORDS ARE INGESTED INTO TRINETX AND THEN THEY'RE SEARCHED.

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THE THING THAT'S MISSING IS THE CONNECTION WITH THE COMPANY RECOGNIZING THAT FOR CERTAIN KINDS OF TRIALS THEY CAN GET SUPPORT FROM CIRM BECAUSE IT WOULD BE -- THEY WOULD FULFILL THE REQUIREMENTS.

CHAIRMAN GOLDSTEIN: OKAY. GREAT. I'M SURE WE'LL ABLE TO RETURN TO SOME OF THESE ISSUES LATER ON IN THIS CALL AND IN SUBSEQUENT CALLS.

BUT THE OTHER PART OF THE PORTFOLIO IS WHAT'S HAPPENING IN CALIFORNIA INDUSTRY AND BEYOND. SHYAM HAS PUT TOGETHER A PRESENTATION. IF SHYAM IS READY, PLEASE GRAB THE SCREEN AND GO AHEAD.

DR. PATEL: THANK YOU, DR. GOLDSTEIN. I'M GOING TO SHARE MY POWERPOINT DECK. I HOPE YOU CAN HEAR ME OKAY.

THE REPORTER: BETH WOULD LIKE FOR THE VOLUME TO BE UP A LITTLE BIT. IT'S A LITTLE BIT HARDER TO HEAR YOU FOR ME.

DR. PATEL: I CAN PROJECT. CAN YOU HEAR ME NOW, BETH?

THE REPORTER: THAT'S BETTER. THANK YOU.

DR. PATEL: SO I'M GOING TO PRESENT CERTAIN SNAPSHOTS FOCUSING ON CELL AND GENE THERAPY DEVELOPMENT IN NEUROLOGICAL DISORDERS. SO THIS IS BY NO MEANS MEANT TO BE COMPREHENSIVE, BUT I WANTED TO GIVE YOU AN IDEA OF CERTAIN AREAS THAT WE'VE BEEN

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TRACKING HERE AT CIRM.

SO I'M GOING TO SKIP THE MISSION SLIDE. AND I'M GOING TO GET TO WHAT WE'LL BE FOCUSING ON. SO I'LL TALK ABOUT INITIALLY WHAT THE PARTNERING STATUS OF THE COMPANIES THAT WE FUND IS. I HAVE SOME EXAMPLES OF THOSE IN HERE. AND THEN CELL THERAPIES FOR PARKINSON'S DISEASE, CELL THERAPIES FOR GLIOBLASTOMA, A SNAPSHOT OF THESE PARTICULAR FIELDS IN THOSE DISEASES.

AS ABLA MENTIONED, GIVEN THE SUCCESS OF LUXTURNA AND ZOLGENSMA, THERE HAVE BEEN SEVERAL COMPANIES THAT HAVE BEEN LAUNCHED FOR AAV GENE THERAPIES FOR MONOGENIC NEURO DISORDERS. I'LL DISCUSS THAT A LITTLE BIT AS WELL. LASTLY, WAYS THAT INDUSTRIES ARE PARTICIPATING IN NONPROFIT GENE THERAPY DEVELOPMENT EFFORTS.

SO I'LL START OFF FIRST, AND THIS IS A BIG TABLE, BUT I'LL START OFF FIRST WITH HOW THE COMPANIES ARE IN OUR PORTFOLIO, WHAT STAGE THEY'RE AT, WHAT SORT OF INDICATIONS THEY'RE TARGETING, AND THEN HOW THEY'RE FUNDED. SO WHAT THIS TABLE IS MEANT TO SHOW YOU IS THAT WE ARE FUNDING -- THESE COMPANIES ARE BEING FUNDED BY CIRM THAT ARE ACROSS ALL STAGES OF DEVELOPMENT FROM DISCOVERY THROUGH PIVOTAL TRIALS. WE'VE SEEN AN UPTICK OF COMPANIES

APPLYING TO AND GETTING FUNDED BY CIRM OVER THE LAST COUPLE YEARS IN PARTICULAR.

SO THESE COMPANIES ARE ACROSS THE WHOLE PORTFOLIO. THEY'RE DEVELOPING CELL AND GENE THERAPIES ACROSS DIFFERENT TECHNOLOGY PLATFORMS FOR VARIOUS DIFFERENT INDICATIONS AS SHOWN ON THIS TABLE. THIS IS A COMPLEMENT TO THE INFORMATION THAT ABLA WAS PRESENTING.

AND THEN THE FUNDING STATUS OF THESE COMPANIES. THE LATER STAGE COMPANIES OBVIOUSLY HAVE MORE VENTURE CAPITAL FUNDING OR PUBLIC MARKET FUNDING. AND THE EARLIER STAGE COMPANIES, THE DISCOVERY STAGE COMPANIES, ARE ALL EITHER GRANT OR SEED STAGE COMPANIES. THEY RAISE SMALL AMOUNTS OF MONEY THROUGH GRANTS AS WELL AS THROUGH SEED STAGE FUNDING.

SO ONE AREA WHERE THERE HAS BEEN A LOT OF ACTIVE INDUSTRY SUPPORT HAS BEEN IN THIS SPECIFIC CASE OF USING PLURIPOTENT STEM CELL-DERIVED PROGENITOR CELLS FOR PARKINSON'S DISEASE. AND SO HERE THERE'S BEEN A NUMBER OF THERAPIES THAT HAVE GONE INTO THE CLINIC, AND ALMOST ALL OF THEM HAVE SOME SORT OF INDUSTRY BACKING. SO THE MOST PROMINENT ONES ARE THE ONES OF DR. LORENZ STUDER AND DR. MALIN PARMAR. BOTH OF THOSE ARE IN THE CLINIC,

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AND THEY'RE ACTUALLY SUPPORTED BY BAYER ON THE STUDER PROJECT AND THEN NOVA NORDISK ON THE PARMAR PROJECT.

SO ON THE STUDER PROJECT, THIS WAS A COMPANY SPUN OUT TO DO THIS, BLUEROCK THERAPEUTICS A FEW YEARS AGO. IT WAS FOUNDED BY BAYER AND VERSANT VENTURES, AND THEN BLUEROCK GOT FULLY ACQUIRED BY BAYER IN 2019. AND THIS TRIAL CONTINUES TO BE SUPPORTED BY BAYER AND BLUEROCK, WHO OPERATES INDEPENDENTLY.

SIMILARLY, IN 2018 NOVA NORDISK STRUCK A PARTNERSHIP WITH LUND UNIVERSITY FOR THEIR EMBRYONIC STEM CELL-DERIVED PROGENITOR CELL THERAPY. AND THIS IS IN CLINICAL TRIALS NOW, AND IT WAS INITIATED LATE LAST YEAR, AND NOVA NORDISK IS FUNDING THAT TRIAL.

THE INTERESTING PART OF THIS IS THAT NEURO COMPANIES, SUCH AS ASPEN NEUROSCIENCE AND RYNE BIO, ARE CONTINUING TO GET ADDITIONAL SUPPORT FROM VENTURE CAPITAL AS THEY PROGRESS THEIR THERAPIES INTO THE CLINIC. SO ASPEN NEUROSCIENCE IS A CALIFORNIA COMPANY. THE DISCOVERY STAGE WORK HERE WAS DONE BY DR. JEANNE LORING, AND IT WAS FUNDED BY CIRM. THE COMPANY WAS SPUN OUT A FEW YEARS AGO. AND IN A TOUGH MARKET ENVIRONMENT IN 2022, IT WENT ON TO RAISE CLOSE TO $150 MILLION IN A SERIES B

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FINANCING FROM BLUE CHIP INVESTORS. AND THEN ALSO RAISED A DEBT FINANCING ROUND IN 2022 TO HELP SECURE SOME OF THE OPERATIONAL CAPITAL THAT IT NEEDS TO CONTINUE TO PROGRESS TO THE CLINIC.

SIMILARLY, RYNE BIO, WHICH IS AN IND-ENABLING COMPANY. THIS WAS RECENTLY FUNDED BY CIRM. IT'S ANOTHER CALIFORNIA COMPANY THAT IS DEVELOPING IPSC-DERIVED NEUROPROGENITOR CELL THERAPY. AND THIS HAS SPUN OUT WITH HELP FROM SAISEI BIO VENTURES AS WELL AS FUJIFILM CDI.

JUMPING ON TO GLIOBLASTOMA, HERE IT'S AN INTERESTING TREND WHERE MOST OF THE CLINICAL STAGE CELL-BASED IMMUNOTHERAPIES ARE ACTUALLY BEING SUPPORTED BY ACADEMIC INSTITUTIONS OR THE NIH. SO CIRM IS CURRENTLY FUNDING SEVEN CELL THERAPY PROJECTS ACROSS TRAN AND CLIN PORTFOLIO FOR GLIOBLASTOMA. ALL OF THEM ARE AT ACADEMIC CENTERS: CITY OF HOPE, STANFORD, AND UCSF.

ONE OF THE CITY OF HOPE PROJECTS WAS LICENSED VERY EARLY ON BY MUSTANG BIO, BUT THE TRIALS ARE BEING SPONSORED BY CITY OF HOPE AT THE MOMENT. EVENTUALLY MUSTANG BIO WILL TAKE THIS PROJECT ON BY COMBINING IT WITH ANOTHER ONCOLYTIC VIRUS THERAPY.

SO GIVEN THE FACT THAT MANY OF THESE

PROJECTS ARE BEING PROGRESSED IN AN ACADEMIC SETTING THROUGH CLINICAL TRIALS, CIRM IS PARTICIPATING WITH VARIOUS DIFFERENT INVESTORS AND FUNDERS TO FIGURE OUT IF THERE'S A BUSINESS MODEL FOR ADVANCING A PORTFOLIO OF THESE THERAPIES FOR GLIOBLASTOMA THROUGH INDUSTRY SUPPORT.

TO FOLLOW ON WHAT ABLA WAS MENTIONING WITH GENE THERAPIES FOR MONOGENIC DISORDERS, AS YOU KNOW, ZOLGENSMA HAS BEEN IN THE MARKET SINCE A FEW YEARS. IT HAS BEEN APPROVED IN 47 COUNTRIES TO DATE. IN OCTOBER OF 2022, THE COMPANY ANNOUNCED THAT THERE WERE TWO PATIENT DEATHS FROM ACUTE LIVER FAILURE. AND THE PRODUCT CONTINUES TO SELL. IT HAS GENERATED $1.37 BILLION IN REVENUE IN THE LAST FISCAL YEAR. THIS IS MOSTLY THROUGH CREATING THE INCIDENT POPULATION.

THERE WAS A RECENT APPROVAL, AS ABLA MENTIONED, OF UPSTAZA, WHICH IS AN AAV GENE THERAPY FOR AADC. THIS WAS APPROVED IN EUROPE.

AND IN RECENT YEARS, BECAUSE OF THE SUCCESS OF ZOLGENSMA AND LUXTURNA, THERE HAVE BEEN SEVERAL COMPANIES LAUNCHED A REALLY SIGNIFICANT VENTURE FINANCING AND PUBLIC MARKET FINANCING TO ADVANCE AAV GENE THERAPIES FOR THESE MONOGENIC NEUROLOGICAL DISORDERS, PARTICULARLY IN

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NEUROMETABOLIC FIELDS, IN NEURODEGENERATIVE FIELDS. HOWEVER, IN THE LAST SEVERAL YEARS, SEVERAL OF THE LATE STAGE CLINICAL PROGRAMS HAVE ENCOUNTERED DIFFICULTIES. I'M GOING TO DESCRIBE SOME OF THOSE IN THE NEXT SLIDE BECAUSE THEY'RE NOT AS SIMPLE AS JUST CLINICAL TRIAL ENDPOINTS NOT BEING MET.

AND THEN BUILDING ON THAT, IN THE PAST COUPLE YEARS THERE HAS BEEN A PUSH TOWARD DEVELOPING AAV ENGINEERING PLATFORMS TO OVERCOME THE SAFETY AND EFFICACY LIMITATIONS FOR CNS GENE DELIVERY. SEVERAL COMPANIES HAVE BEEN LAUNCHED, AND THERE'S VERY ACTIVE INVESTMENT AND PARTNERSHIP FROM BIOPHARMA INVESTORS, AND I'LL TOUCH ON THAT IN A COUPLE SLIDES.

SO TO GET TO THE POINT OF COMPANIES THAT HAVE BEEN DEVELOPING GENE THERAPIES FOR MONOGENIC DISORDERS, SEVERAL OF THEM HAVE BEEN IN LATE STAGE. THIS SLIDE SHOWS YOU A COMPILATION OF SOME OF THESE EXAMPLES. SO LYSOGENE AND SIO GENE THERAPIES WERE BOTH COMPANIES THAT WERE ADVANCING AAV GENE THERAPIES. THEY WERE IN LATE STAGE, AND BOTH OF THOSE COMPANIES ARE CURRENTLY IN BANKRUPTCY PROCEEDINGS.

IN THE CASE OF SIO GENE THERAPIES, THIS COMPANY HAD CANCELED ITS PARKINSON'S DISEASE

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PROGRAM, AND IT'S GM1 AND GM2 PROGRAMS ARE BEING RETURNED TO U MASS.

THERE ARE ALSO A COUPLE OF OTHER COMPANIES THAT HAVE LAUNCHED ALONG THAT TIME FRAME. THERE WAS TAYSHA GENE THERAPIES WHICH HAD LAUNCHED EARLY ON WITH SIGNIFICANT VENTURE BACKING, AND IT WENT PUBLIC. AT ONE POINT IT HAD AGGREGATED OVER 20 DIFFERENT PROGRAMS, ALL BEING PROGRESSED THROUGH PARTNERSHIP WITH PATIENT GROUPS AS WELL AS NIH AND OTHER FUNDING AGENCIES. AND IT DROPPED MOST OF THOSE AND KEPT GAN AND RETT SYNDROME PROJECTS. IN THE LAST QUARTER OF 2022, IT STRUCK A DEAL WITH ASTELLAS TO GET $50 MILLION TO ADVANCE THOSE TWO THERAPIES TO CLINICAL DEVELOPMENT, AND IT HAD SEVERAL LEADERSHIP CHANGES. THIS IS A COMPANY THAT'S GOING THROUGH A LOT OF FLUX, AND IT USED THE ASTELLAS FUNDING TO PROGRESS THE THERAPY GOING FORWARD.

PREVAIL THERAPEUTICS WAS A COMPANY THAT HAS BEEN ACQUIRED EARLY ON BY LILLY, AND IT IS CONTINUING TO ADVANCE A NUMBER OF GENE THERAPIES INTO THE CLINIC.

THE LAST THING I WANT TO POINT OUT, UNIQURE, WHICH IS A COMPANY THAT RECENTLY GOT A BLA FOR HEMGENIX, WHICH IS FOR BLOOD DISORDERS, BUT IT

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ALSO IS PROGRESSING SEVERAL DIFFERENT NEUROLOGICAL DISORDER CANDIDATES, INCLUDING ONE FOR ALS THAT IT ACQUIRED FROM APIC BIO THAT WENT INTO THE CLINIC. IT'S ACTIVELY RECRUITING NEW PROJECTS AND PROGRESSING ITS OWN PIPELINE. AND, PRESUMABLY, HAVING A COMMERCIAL STAGE PROJECT IS GOING TO BENEFIT THIS COMPANY IN TERMS OF ITS REVENUE.

SO AS I MENTIONED, THERE ARE SEVERAL COMPANIES THAT ARE DEVELOPING NEW TECHNOLOGIES FOR AAV. THESE INCLUDE CAPSIDA ENGINEERING AS WELL AS GENETIC ENGINEERING. I WANT TO HIGHLIGHT A FEW OF THESE TO SHOW YOU SOME TRENDS.

SO A FEW YEARS AGO SEVERAL COMPANIES WERE LAUNCHED TO USE AI-DRIVEN CAPSIDA ENGINEERING TECHNOLOGY. THESE ARE SHAPE THERAPEUTICS AND DYNO ARE TWO EXAMPLES HERE. AS YOU CAN SEE, BOTH WERE PARTNERED WITH ROCHE FOR PRETTY LARGE BIOPHARMA, BIO BUCKS DEALS. THEY'VE ALSO RAISED SIGNIFICANT VENTURE CAPITAL FUNDING IN 2019, 2021 WHERE IT WAS RELATIVELY EASY TO RAISE SUCH CAPITAL.

THERE WERE SOME COMPANIES, SUCH AS AFFINIA, APERTURA, THAT ARE TAKING A BROADER APPROACH. NOT ONLY ARE THEY ENGINEERING NEW CAPSID, THEY'RE ALSO ENGINEERING NEW PROMOTERS AND REGULATORY ELEMENTS TO BOTH IMPROVE THE TARGETING AS

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WELL AS THE EXPRESSION OF THOSE GENES ONCE THEY'RE IN THE CELLS. BOTH OF THOSE COMPANIES HAVE RAISED SIGNIFICANT VENTURE CAPITAL FINANCING IN THE LAST FEW YEARS.

THE LAST COMPANY ON THIS LIST IS A VERY FOCUSED APPROACH. IT IS DEVELOPING CAPSIDS THAT PENETRATE THE BLOOD BRAIN BARRIER FOR I.V. DELIVERY OF GENE THERAPIES FOR NEUROLOGICAL DISORDERS. THIS COMPANY HAS GONE ON TO HAVE SIGNIFICANT BIOPHARMA PARTNERSHIPS BECAUSE IT WAS A VERY UNIQUE AND FOCUSED PLATFORM, INCLUDING WITH ABBVIE, CHRISPR THERAPEUTICS, AND PREVAIL, WHICH IS THE LILLY COMPANY MORE RECENTLY.

ONE AREA THAT'S SOMEWHAT ENCOURAGING IS THAT THERE A LOT OF DIFFERENT NONPROFIT AS WELL AS CONSORTIA APPROACHES TO DEVELOPING RARE DISEASE GENE THERAPIES FOR NEUROLOGICAL DISORDERS. THERE'S THE AMP BGTC THAT CIRM PARTICIPATES IN. THIS IS THE ACCELERATING MEDICINES PARTNERSHIP, BESPOKE GENE THERAPY CONSORTIUM. IT'S A COLLABORATION BETWEEN NIH, FDA, AND OVER 20 INDUSTRY PARTNERS TO DEVELOP A BLUE BOOK TO PROGRESS GENE THERAPIES THAT ARE IN ULTRA RARE DISEASES FROM PRE-IND THROUGH PHASE 1 CLINICAL TRIALS. AND MANY OF THE INDICATIONS THAT PRESUMABLY FALL INTO THIS CATEGORY ARE GOING TO BE

NEUROLOGICAL DISORDERS.

SIMILARLY, THERE ARE OTHER GROUPS SUCH AS CURESPG50, COLUMBUS CHILDREN'S FOUNDATION, ODYLIA, AND MILA'S MIRACLE FOUNDATION, ALL OF WHICH ARE DEVELOPING DIFFERENT TYPES OF GENE THERAPIES FOR THESE RARE DISEASES.

ONE THING I WANT TO NOTE ON THIS SLIDE IS THAT A LOT OF THESE GROUPS ARE RELYING ON INDUSTRY PARTNERS TO BE ABLE TO PROGRESS THESE BESPOKE THERAPIES THROUGH PRE-IND, IND-ENABLING STUDIES, AS WELL AS CLINICAL TRIALS.

A LOT OF THESE INDUSTRY GROUPS ARE PROVIDING THESE SERVICES AS IN-KIND, DISCOUNTED SERVICES, OR THEY'RE PROVIDING SPECIALIZED ACCESS TO THOSE PROJECTS. HERE ARE SOME EXAMPLES OF THOSE. FOR EXAMPLE, CHARLES RIVER LABS, WHICH IS A MAJOR CONTRACT RESEARCH ORGANIZATION AND A MANUFACTURING ORGANIZATION, IS PROVIDING ANIMAL MODELS, TESTING, AND IND SERVICES TO SEVERAL DIFFERENT NONPROFIT GROUPS DEVELOPING THESE RARE DISEASE GENE THERAPIES.

SIMILARLY, CONTRACT MANUFACTURING ORGANIZATIONS SUCH AS VIRALGEN, WHICH IS OWNED BY BAYER, AND ANDELYN, WHICH WAS SPUN OUT FROM NATIONWIDE CHILDREN'S HOSPITAL, ARE ALSO PROVIDING MANUFACTURING SERVICES TO THESE GROUPS. OFTENTIMES

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IT CAN INCLUDE IN-KIND MANUFACTURING, DISCOUNTED MANUFACTURING, AND SO ON.

LASTLY, I WANT TO END ON NOTING THE CHALLENGE FOR DEVELOPING THERAPIES FOR ALZHEIMER'S DISEASE. AND SO THIS WAS A STUDY THAT WAS CONDUCTED SHORTLY AFTER ADUCANUMAB WAS APPROVED, ADUHELM FROM BIOGEN. AND SO IT ESTIMATED THAT THERE WERE ABOUT 235 AGENTS FOR ALZHEIMER'S DISEASE TO ENTER INTO CLINICAL DEVELOPMENT BETWEEN 1995 AND 2021. AND OF THOSE, SIX WERE COMMERCIALIZED, INCLUDING ADUCANUMAB. AND SO THEY HAD CALCULATED BASED ON THAT THE FAILURE RATE WAS 95 PERCENT. AND THEN IT WENT ON TO CALCULATE HOW MUCH INDUSTRY FUNDING HAS ACTUALLY GONE INTO THIS BASED ON ESTIMATIONS OF WHAT IT COSTS TO DO PHASE 1, 2, AND 3 CLINICAL TRIALS FOR ALZHEIMER'S DISEASE CANDIDATES. AND IT ESTIMATED ABOUT $42.5 BILLION IN INDUSTRY FUNDING HAS GONE INTO THIS FIELD SINCE 1995 THROUGH 2021. AND IT LAYS OUT SOME OF THOSE COST STRUCTURES THERE OF PHASE 1 TO PHASE 3 COSTS OUT OF POCKET TO BE $462 MILLION.

SO BASED ON THESE CALCULATIONS, THERE WAS A 2014 PAPER THAT ESTIMATED THAT IT TAKES ABOUT 13 YEARS AND $5.7 BILLION TO MARKET AN ALZHEIMER'S DISEASE DRUG CANDIDATE. NOW, I WANT TO BREAK THAT

NUMBER DOWN A LITTLE BIT. SO YOU'VE SEEN NUMBERS THAT ARE AROUND 1.5 OR $2 BILLION OF DRUG DEVELOPMENT COST FOR A PARTICULAR DRUG. SO WHAT THOSE NUMBER BAKE INTO THAT IS THE FACT THAT THERE'S THE OUT-OF-POCKET COSTS OF PRECLINICAL AND CLINICAL DEVELOPMENT PLUS FACTORING INTO THE FAILURE RATE AT EACH OF THOSE STAGES, SO PRECLINICAL, PHASE 1, PHASE 2, PHASE 3, AND THEN THE COST OF CAPITAL. SO BASICALLY A DISCOUNTED RATE APPLIES TO THAT FOR WHAT IS THE COST OF DEDICATING ALL THAT CAPITAL TO THAT PROJECT FOR THAT NUMBER OF YEARS. THAT'S THE 1.5 TO $2 BILLION.

BECAUSE OF THE FAILURE RATE ASSOCIATED WITH ALZHEIMER'S DISEASE, THAT NUMBER SHOOTS UP TO $5.7 BILLION ESTIMATE FOR THIS PARTICULAR FIELD BECAUSE OF THE LARGE NUMBER OF FAILURE RATES HAPPENING AT PHASE 1, 2, AND 3 CLINICAL TRIALS.

ONE OF THE THINGS THAT THIS PAPER HIGHLIGHTS IS THAT THE RATE OF GROWTH IN R&D SPENDING HAS SLOWED IN RECENT YEARS. AND IT HAS A CHART IN THERE SHOWING THAT. I DIDN'T PUT IT ON HERE. BUT MORE RECENTLY THERE HAVEN'T BEEN AS MANY CLINICAL TRIALS IN ALZHEIMER'S DISEASE DRUG CANDIDATE DEVELOPMENT.

ONE THING I DO WANT TO NOTE IS THAT THIS

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DOES NOT INCLUDE LEQEMBI WHICH WAS APPROVED AFTER THE PAPER WAS PUBLISHED.

IN SUMMARY, JUST GOING TO SUMMARIZE ALL THE SLIDES I PRESENTED SO FAR. SO FIRST OF ALL, THE BIOTECH COMPANIES THAT CIRM FUNDS IN NEUROLOGY TEND TO SPAN ALL STAGES OF DEVELOPMENT AND FINANCING. AND THEN ON THE REALLY SPECIFIC FIELD OF PLURIPOTENT STEM CELL-BASED CELL THERAPIES FOR PARKINSON'S DISEASE, THERE CONTINUES TO BE STRONG INDUSTRY AND ACADEMIC COLLABORATIONS THAT ARE DRIVING THOSE INTO THE CLINIC.

PRECLINICAL AND CLINICAL DEVELOPMENT OF CELL-BASED THERAPIES FOR GLIOBLASTOMA ARE BEING DRIVEN BY ACADEMIC INSTITUTIONS, AND WE ARE CURRENTLY FUNDING EIGHT SUCH PROGRAMS.

WHILE SOME LATE STAGE AAV GENE THERAPY COMPANIES HAVE FACED RECENT FINANCIAL DIFFICULTIES, THE INDUSTRY CONTINUES TO SUPPORT NEW BIOTECHS DEVELOPING ENGINEERING PLATFORMS TO IMPROVE AAV SAFETY AND EFFICACY.

AS I MENTIONED, THERE ARE SEVERAL NONPROFIT MODELS THAT ARE PROGRESSING AAV GENE THERAPIES FOR RARE DISEASES TO THE CLINIC. AND THEY'RE DOING SO IN PARTNERSHIP WITH INDUSTRY CRO'S AND CDMO'S.

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AND THEN LASTLY, OVER 25 YEARS OF INVESTING IN CLINICAL DEVELOPMENT OF ALZHEIMER'S DISEASE TREATMENTS HAS RESULTED IN ONLY SEVEN FDA-APPROVED TREATMENTS TO DATE.

SO WITH THAT, I'LL PAUSE MY PRESENTATION. THANK YOU.

CHAIRMAN GOLDSTEIN: THANK YOU VERY MUCH, SHYAM. THAT WAS INCREDIBLY HELPFUL.

SO THIS WAS DESIGNED TO GIVE US A SENSE OF WHAT THE COMMERCIAL AND ACADEMIC LANDSCAPE IN CALIFORNIA IS LIKE INDEPENDENT OF CIRM FUNDING FOR THE MOST PART. THIS WILL HELP US AS WE THINK ABOUT PLANNING. SO QUESTIONS FOR SHYAM. MAYBE I'LL MAKE A COMMENT. SO PREDICTING THE FUTURE IS ALWAYS A DODGY BUSINESS. I'LL COME BACK TO THAT. J.T., GO AHEAD.

DR. THOMAS: THANKS VERY MUCH, SHYAM. JUST CURIOUS. THERE'S SOME SORT OF NOTABLE ABSENCES OF COMPANIES DEALING WITH CERTAIN NEUROLOGICAL DISORDERS. MAYBE I MISSED IT, BUT HUNTINGTON'S, FOR EXAMPLE, WHAT ARE THE -- WHAT'S SORT OF THE INDUSTRY TAKE THESE DAYS ON THE LIKELIHOOD OF GETTING COMPANIES DEALING WITH THOSE NEUROLOGICAL DISORDERS THAT CURRENTLY DON'T HAVE ANY TAKERS BECAUSE OF THE R&D DIFFICULTIES, ET CETERA? WHAT'S PROVING --

OBVIOUSLY ALZHEIMER'S HAS HAD ALL SORTS OF PROBLEMS. WHAT ELSE IS PROVING TO BE HUGELY PROBLEMATIC AT THIS STAGE OF THE GAME?

DR. PATEL: SO I WOULD GO BACK TO THE SLIDE AROUND THE AAV GENE THERAPIES FOR RARE DISEASES. IN THOSE INSTANCES, SEVERAL OF THE COMPANIES THAT I LISTED OFF ON THAT PRESENTATION WERE COMPANIES THAT HAVE PRETTY GOOD CLINICAL DATA AND ARE CONTINUING TO GET POSITIVE SIGNALS IN THEIR TRIALS. AND THEY WERE JUST NOT ABLE TO RAISE ADDITIONAL FUNDING FROM EITHER THE PUBLIC OR PRIVATE CAPITAL MARKETS BECAUSE OF THE COST IT'S GOING TO TAKE TO GET THOSE TO APPROVAL THROUGH THE REGULATORY PATHWAY. SO I THINK THAT'S BEEN ONE OF THE CHALLENGES, THIS SORT OF DYNAMIC OF DOING QUICK TRIALS TO GET THESE THERAPIES TO APPROVAL MAY NOT BE AS QUICK AS WAS ORIGINALLY ESTIMATED A FEW YEARS AGO.

I DON'T KNOW IF, ROSA, YOU WANT TO ADD TO THAT.

DR. CANET-AVILES: THANK YOU, SHYAM. THERE ARE TWO OTHER ELEMENTS TO CONSIDER. ONE IS THAT, FOR EXAMPLE, FOR ALZHEIMER'S DISEASE, THERE'S ALWAYS BEEN THE PATHWAY; HOWEVER, THERE ARE OTHER MECHANISMS OF DISEASE THAT WE HAVE NOT BEEN

TARGETING IN THESE THERAPIES. SO THAT'S ONE PART WHERE THERE CAN BE INVESTMENT. AND THE COMPANIES RELY ON EARLY ACADEMIC RESEARCH TO FUND.

ANOTHER THING IS THE DEVELOPMENT OF BIOMARKERS, FOR EXAMPLE, THAT HELP US STRATIFY THE POPULATION SO THAT WE CAN HAVE EFFECTIVE CLINICAL TRIALS. SOMETIMES (UNINTELLIGIBLE) BECAUSE WE HAVEN'T ACTUALLY STRATIFIED THE POPULATIONS CORRECTLY.

AND ANOTHER PLACE WHERE THERE CAN BE INVESTMENT IS IN THE DEVELOPMENT OF DELIVERY MECHANISMS, THE WHOLE DELIVERY TO THE BRAIN. AND TARGETING THE RIGHT CELL TYPES IS ANOTHER PLACE. SO THOSE ARE PLACES WHERE I THINK THERE IS A NICHE FOR CIRM TO INVEST, BUT IT'S MORE EARLIER IN THE PART. AS DR. GOLDSTEIN MENTIONED, THIS IS NOT THE TOPIC OF TODAY.

DR. CREASEY: IF I CAN ECHO WHAT ROSA SAID, WHEN IT COMES TO CLINICAL MECHANISMS, NEW TECHNOLOGIES FOR DRUG DELIVERY ARE VERY IMPORTANT IN AREAS WHERE HOW DO YOU REACH TO THE RIGHT CELL AND THE RIGHT PART OF THE BRAIN. AND THAT KIND OF TECHNOLOGY WILL DO WELL FOR US FOR THE PATIENT.

FORMULATION OF THE MATERIALS. AGAIN, SO IT'S NOT -- MECHANISM IS IMPORTANT, KNOWING EXACTLY

WHAT CELL IS INVOLVED IN WHAT PART OF THE BRAIN, AND HOW TO GET THE THERAPY THERE. AND THAT WILL WORK WELL WITH ALMOST -- AND, AGAIN, WITH APPROPRIATE BIOMARKERS, AGAIN, WITH THE STRATIFYING THE PATIENTS. BUT I THINK THE PATH IS TO VALIDATE THE BIOMARKERS AND SHOW THAT THEY ARE ACTUALLY EXISTING IN THE HUMAN POPULATION AND THEN REPEAT THAT CYCLE AND DEMONSTRATE THE VALUE OF THAT KIND OF EVALUATION OF THE WHOLE CIRCLE.

CHAIRMAN GOLDSTEIN: FRED. PLEASE.

DR. FISHER: I APOLOGIZE. I'M FEELING A LITTLE LOST AT THE MOMENT. FORTUNATELY, WE DON'T HAVE TO GO THROUGH THE GYMNASTICS THAT PHARMA GOES THROUGH TO JUSTIFY THE COST OF DEVELOPING DRUGS. WE DON'T ALLOW OUR APPLICANTS TO LOAD IN THE COST OF BUYER FAILURES INTO WHAT THEY'RE GOING TO PUT INTO THEIR CIRM BUDGETS.

SO I NEED HELP UNDERSTANDING -- CONNECTING THE DOTS REALLY BETWEEN WHAT IT IS YOU'RE PRESENTING TO US AND HOW IT HELPS THIS GROUP MOVE FORWARD WITH OUR TASK. AND, AGAIN, I APOLOGIZE IF I'M JUST BEING THICK ABOUT IT, BUT IT'S ALL SEEMING LIKE WAY OFF POINT FOR US TO BE TALKING ABOUT SOME OF THIS STUFF.

CHAIRMAN GOLDSTEIN: SO WHY DON'T I HANDLE THAT ONE BECAUSE THAT'S ON ME. WE HAVEN'T DONE AN

ADEQUATE JOB EXPLAINING WHY WE'RE GOING THROUGH THIS. I THINK THE REASON IT'S RELEVANT, FRED, IS THAT CIRM DOESN'T EXIST IN A VACUUM. WE ARE SURROUNDED BY ACTIVE FINANCING OF A VARIETY OF COMPANIES DOING RESEARCH IN THE FIELD.

I THINK ONE POINT WOULD BE THERE IS A LOT OF MONEY INVESTED FROM THE PRIVATE SECTOR CURRENTLY. AND, TWO, IT'S NOT OBVIOUS TO ME, AT LEAST, THAT THE PRIVATE SECTOR PRIORITIES ARE RADICALLY DIFFERENT THAN CIRM PRIORITIES. WHAT IS DIFFERENT IS COST OF CAPITAL AND THE DEGREE OF DIFFICULTY THAT AFFECTS US ALL IN PROGRESSING THERAPIES. SO IT'S NOT THE CASE THAT INDUSTRY SOMEHOW IS INVESTED IN COMPLETELY DIFFERENT AREAS THAN WHAT CIRM IS LOOKING AT. I THINK WE ARE ALL IN A SENSE LOOKING UNDER THE STREETLIGHT WHERE WE THINK THERE ARE CURRENT OPPORTUNITIES. AND I DON'T THINK THAT INDUSTRY HAS FOUND THINGS THAT CIRM HASN'T FOUND AND VICE VERSA.

THERE'S NO HIDDEN PORTFOLIO OUT THERE WOULD BE THE POINT, I THINK. I HOPE THAT HELPS YOU.

DR. FISHER: WELL, I CERTAINLY AGREE WITH THAT STATEMENT. AND THANK YOU.

CHAIRMAN GOLDSTEIN: OKAY. GLAD TO BE OF USE.

DR. FISHER: THERE'S NO WORSE PLACE TO PUT

MONEY IF YOU'RE A DRUG DEVELOPER OTHER THAN NEURODEGENERATIVE DISEASE. IT'S BEEN PROVEN OVER AND OVER. THE FAILURE RATE FOR ALS, FOR EXAMPLE, WHICH I KNOW A LITTLE BIT ABOUT, LIKE YOU'RE ALMOST GUARANTEED TO LOSE YOUR SHIRT PUTTING ANY MONEY INTO ALS THERAPY DEVELOPMENT BECAUSE 99.999 TIMES OUT OF A HUNDRED YOUR PHASE 2 OR PHASE 3 TRIAL WILL FAIL. IT'S JUST THE TRACK RECORD.

SO THE FACT THAT CIRM CAN PLAY AN EARLY STAGE DERISKING ROLE, NOT JUST WITH ALS, BUT OTHER DISEASES, IS HUGE LEVERAGE THAT THOSE COMPANIES CAN USE. I THINK WE ALREADY KNOW THAT OURSELVES, AND I THINK WE ALREADY KNOW THAT ABOUT THE SPACES WE ARE WORKING IN. AND I'M GRATEFUL THAT THE VOTERS OF CALIFORNIA PROVIDED THE MONEY TO DO THE WORK TO AS MUCH AS POSSIBLE DERISK THE ENORMOUS COST TO THE PRIVATE SECTOR FOR DEVELOPING THESE DRUGS.

CHAIRMAN GOLDSTEIN: GREAT POINT, FRED. THAT'S VERY HELPFUL.

I'D ALSO JUST MENTION IN PASSING RAISING CAPITAL IS MORE DIFFICULT IN THE EARLY STAGES, FOR EXAMPLE, AND WE MAY SEE AN INCREASE IN APPLICATIONS THERE. LAUREN.

MS. MILLER-ROGEN: THE ALZHEIMER'S HILL THAT WE'RE ALL CLIMBING IS CERTAINLY STEEP AND FULL

OF HEAVY BOULDERS, BUT STILL WE CLIMB. AND I HAD A CALL ACTUALLY EARLIER TODAY WITH PEOPLE FROM THE BILL GATES FOUNDATION, WHO ARE OBVIOUSLY VERY FOCUSED ON ALZHEIMER'S, BUT SPECIFICALLY THOUGHT I WOULD MENTION IT. I DON'T KNOW IF WE'VE CONNECTED WITH THEM ON THEIR WORK, BUT THEY'RE VERY SPECIFICALLY INTERESTED. I'LL JUST READ IT TO MAKE SURE I'M GETTING IT CORRECTLY. THEY FOCUS ON BIOMARKER DEVELOPMENT AND NOVEL DIAGNOSTIC TECHNOLOGIES THAT WILL AID IN ALZHEIMER'S DISEASE, YADA, YADA, LIKE BLOOD TESTS, EYE SCANS, DIGITAL TOOLS, ET CETERA.

SO I WONDERED IF THERE HAD BEEN DISCUSSION ABOUT POTENTIALLY ANY OF THEIR WORK BEING DONE IN CALIFORNIA AND COLLABORATIONS ON THAT END BECAUSE THEY'RE CERTAINLY VERY DEDICATED TO THAT PARTICULAR DISEASE AND PROGRESS IN THAT.

CHAIRMAN GOLDSTEIN: I THINK THAT --

DR. CANET-AVILES: CAN I ADD? WE HAD AN INITIAL -- AS YOU RECALL, LAUREN, WE HAD A WORKSHOP LAST YEAR IN FEBRUARY WHERE WE INVITED MEMBERS FROM THE CENTRAL NERVOUS SYSTEM CONSORTIUM TO TALK ABOUT WHAT THE FUTURE OF CIRM COULD BE IF WE WERE GOING TO DO COLLABORATIVE DATA, THE STRUCTURE. AND ONE OF THE THINGS THAT THE GATES FOUNDATION HAS BEEN DOING,

THEY DEVELOPED THE ALZHEIMER'S DISEASE WORKBENCH, WHICH IS A NEW PLATFORM THAT THEY ARE COLLABORATING WITH DIFFERENT GROUPS TO LEVERAGE DATA TO FURTHER THE DEVELOPMENT OF ALZHEIMER'S DISEASE AND RELATED DEMENTIAS. WE HAD PATRICK BRANNELLY AND SOMEBODY ELSE.

SO WE HAVE INTERACTED WITH THEM, AND THESE ACTUALLY COULD BE A GOOD POINT TO BRING UP WHEN WE TALK ABOUT EARLIER DISCOVERY CONSORTIA TYPE AND MULTIDISCIPLINARY THINGS TYPE OF THINKING THAT WE'VE KIND OF MENTIONED BEFORE AND DR. GOLDSTEIN MIGHT BRING AT A LATER STAGE.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU VERY MUCH, ROSA. THAT'S HELPFUL.

SO I THINK WE ARE, FOR THE MOMENT AT LEAST, ADEQUATELY INFORMED ON BACKGROUND FROM CIRM. I'LL JUST POINT OUT THAT PRIOR TO SEEING THE INFORMATION THAT CIRM HAS ACCUMULATED, I HAD WONDERED WHETHER THERE'S SOME MISSING PART OF NEURODEGENERATION IN PARTICULAR THAT WE WERE MISSING. I DON'T THINK THAT THERE'S ANY EASY WINS THAT I SEE IN NEURODEGENERATION, AT LEAST AT THE MOMENT, BUT THE WORK NEEDS TO CONTINUE.

SO THAT BRINGS ME TO THE TOPIC OF HOW SHOULD WE PROCEED AS A TASK FORCE IN OUR PLANNING IN

TERMS OF STRUCTURE AND WHERE SHOULD WE FOCUS. MY INITIAL THOUGHT WHEN THE TASK FORCE WAS FIRST CREATED WAS THAT WE SHOULD HOLD A SERIES OF LONG MEETINGS BETWEEN NOW AND THE END OF JUNE SO AS TO DEVELOP A COMPLETE PLAN FOR A BILLION AND A HALF DOLLARS BY THE END OF JUNE FOR THE ICOC TO CONSIDER AND THEN PASS.

TWO FACTORS HAVE MADE ME THINK THAT I WAS COMPLETELY WRONG ABOUT THAT APPROACH. ONE IS THE KIND OF INFORMATION THAT ROSA AND SHYAM JUST PRESENTED, WHICH, AS I JUST MENTIONED, I DON'T THINK THAT THERE'S A MISSING PART OF NEURODEGENERATION THAT WE'RE NOT ADEQUATELY INVESTED IN. IF SOMEBODY CAME FORWARD WITH A NEW, INTERESTING PROPOSAL IN THAT AREA, WE, CIRM, WOULD JUMP ON IT.

SO I THINK WHAT I WOULD CALL THE FORCED MARCHED PLAN, TO TRY TO GET ALL THE PLANNING DONE BY THE END OF JUNE, IS PROBABLY REALLY NOT WORKABLE GIVEN PEOPLE'S SCHEDULES AND OTHER COMMITMENTS.

THE OTHER POSSIBILITY THAT I'VE DISCUSSED WITH SOME FOLKS AT CIRM AND WITH SOME OUTSIDE GROUPS IS, WHEN YOU LOOK AT THE CIRM PORTFOLIO AND TO A LESSER EXTENT THE INDUSTRY PORTFOLIO, IT IS CLEAR TO ME, AT LEAST, AND SOME OTHERS, THAT WE ARE NOT ADEQUATELY INVESTED IN NEUROPSYCHIATRIC DISORDERS.

THESE ARE A COLLECTION OF, AS YOU KNOW, DEVASTATING DISORDERS THAT OFTEN HIT EARLY IN LIFE AS IN THE CASE OF SCHIZOPHRENIA AND WHERE THERE'S QUITE A BIT OF EVIDENCE THAT THERE ARE SUBSTANTIAL GENETIC CONTRIBUTIONS TO THOSE DISORDERS. OPIOID USE DISORDERS IS ANOTHER ONE THAT ACTUALLY FITS THAT BILL TO MY SURPRISE THAT I'VE LEARNED ABOUT WHERE THERE IS SIGNIFICANT GENETIC CONTRIBUTIONS.

AND THE REASON I BRING THAT UP IS THAT DISEASE MODELING IN STEM CELLS AND THEN PROGRESSION USING STEM CELLS IS QUITE A BIT MORE STRAIGHTFORWARD IN MANY CASES IF THERE ARE SUBSTANTIAL GENETIC CONTRIBUTIONS. NOW, OBVIOUSLY THAT'S NOT TRUE IN THE CASE OF INJURY OR STROKE TO MY KNOWLEDGE. BUT IT LEADS ME TO SUGGEST THAT, RATHER THAN TRYING TO PLAN THE ENTIRE $1.5 BILLION IN THE NEXT SIX MONTHS OR FOUR MONTHS ACTUALLY AT THIS POINT, THAT WE INSTEAD DEVOTE OUR ATTENTION TO AREAS WHERE WE THINK CIRM MAY BE UNDERINVESTED IN AT THE MOMENT AND SEE IF WE CAN DEVELOP A WORKABLE PLAN MOVING FORWARD. AND THEN FOLLOWING THE JUNE ICOC MEETING, WHERE I WOULD HOPE WE WOULD GET APPROVAL OF SUCH A PLAN FOR NEUROPSYCHIATRIC DISORDERS, TO THEN THINK ABOUT TACKLING NEURODEGENERATIVE DISORDERS TO SEE IF THERE'S SOMETHING MISSING, ALTHOUGH I SUSPECT THAT

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THERE'S NOT A BIG HOLE IN THE CIRM PORTFOLIO.

SO THOSE ARE THE TWO MAIN WAYS OF PROCEEDING, I THINK. AND LET'S SEE IF PEOPLE HAVE DISCUSSION POINTS, QUESTIONS, OR COMMENTS ABOUT PROCEEDING WITH THE NOTION OF LET'S TAKE AN AREA WHERE WE ARE UNDERINVEST, SUCH AS NEUROPSYCHIATRIC, DO OUR PLANNING WORK THERE TO START, WHICH WILL BE A PART OF THE ONE AND A HALF BILLION, BUT NOT THE ENTIRE ONE AND A HALF BILLION, AND THEN COME BACK TO SOME OF THESE OTHER AREAS. THOUGHTS? PAT.

DR. LEVITT: SO I THINK THE HOLE IS IN LARGE PART DUE TO THE VERY DIFFERENT LEVEL OF CHALLENGE, SCIENTIFIC CHALLENGE, AND COMPLEXITY, HETEROGENEITY, SINGLE GENE DISORDERS THAT IN PSYCHIATRY ARE RARE. AND SO IT'S MULTIGENIC, WHICH MAKES IT REALLY CHALLENGING IN TERMS OF GENE THERAPY. SO PEOPLE ON THIS CALL CAN GO THROUGH A PLETHORA OF WHAT THE CHALLENGES ARE.

I DON'T DISAGREE WITH TRYING TO COME UP WITH A PLAN THAT INCLUDES THAT BECAUSE IT'S WOEFULLY UNDERSOURCED NOW. NOT BECAUSE CIRM DOESN'T WANT TO DO IT, BUT BECAUSE THERE'S JUST NOT ENOUGH ACTIVITY THERE THAT RECOGNIZES THE OPPORTUNITIES THAT CIRM PROVIDE, WHETHER IT'S DISCOVERY OR SOMETHING MORE ADVANCED.

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WHEN YOU SAY WE'RE NOT UNDERRESOURCED IN TERMS OF NEURODEGENERATION, WHEN I HEAR THAT OUR PORTFOLIO'S ABOUT A LITTLE BIT LIKE 10 OR 11 PERCENT OF THE $1.41 BILLION, AND IT'S MOSTLY FOCUSED ON NEURODEGENERATION, CANCER, AND SOME OCULAR COMPONENTS, THOSE ARE ALL GREAT. I DON'T THINK WE'RE GOING TO MAKE UP THE OTHER 90 PERCENT WITH FOCUSING ON NEUROPSYCHIATRIC DISORDERS. SO I DO THINK THAT HAVING A BROADER PERSPECTIVE AND RECOGNIZING THAT, AND $1.4 BILLION IS A LOT OF MONEY, AND WE ARE NOT EVEN CLOSE TO THERE YET EVEN WITH THE FOCUS IN AREAS THAT SEEM MORE AMENABLE OR MORE TRACTABLE.

SO I THINK I WOULD CAUTION AGAINST BEING REALLY FOCUSED IN AN AREA WHICH EVERYBODY AGREES IS INCREDIBLY DIFFICULT. EVEN AT THE BASIC SCIENCE LEVEL, IT'S INCREDIBLY DIFFICULT.

CHAIRMAN GOLDSTEIN: FAIR ENOUGH, PAT. I THINK MY POINT WOULD BE, NOT THAT THAT WOULD BE OUR ONLY ACTIVITY INDEFINITELY, BUT WE HAVE TO START SOMEWHERE, I THINK. AND SO TAKING A BITE OUT OF AN AREA WHERE WE'RE UNDERINVESTED HAS STRUCK ME AND SOME OTHERS AS A USEFUL THING TO DO. AL.

MR. ROWLETT: CERTAINLY THE AREA OF NEUROPSYCHIATRIC DISORDERS AND POTENTIALLY A STUDY

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THAT MODELS IPSC CELLS AND SCHIZOPHRENIA, WHILE UNDERSTANDING THAT MY HOPE WOULD BE THAT AT SOME POINT CIRM COULD FUND SUCH A STUDY, I RECOGNIZE THAT THERE'S AN EXTRAORDINARILY DIFFICULT LIFT WITH THAT. AND YET, I ALSO UNDERSTAND THAT, AS A PATIENT ADVOCATE, WHEN I SPEAK TO THE CITIZENS IN THE AREA OF NEUROPSYCHIATRIC DISORDERS THAT I GET TO WORK WITH ALL THE TIME, THAT'S ONE OF THE QUESTIONS THEY WOULD ASK ME. SO WHAT WORK ARE YOU DOING TO ADVANCE STUDIES THAT AMELIORATE OR ADDRESS SCHIZOPHRENIA BECAUSE IT'S SO DEVASTATING?

AND THEY CAN ARTICULATE IT VERY PLAINLY AND SIMPLY, THAT SCHIZOPHRENIA HAS A DEVASTATING EFFECT ON PATIENTS, ON FAMILIES, ET CETERA. AND SO I AM ENTHUSIASTICALLY IN SUPPORT OF THAT. AND MAYBE EVEN, AS I THINK ABOUT WHAT MARV SAID ABOUT AN HOUR AGO, DOUBLE DOWNING ON SOME OF HIS NOTIONS ABOUT NEUROPSYCHIATRIC DISORDERS. YES, LARRY, YOU'VE GOT MY ENTHUSIASTIC SUPPORT ABOUT THAT PLAN.

CHAIRMAN GOLDSTEIN: THANK YOU, AL. MARK. YOUR HAND'S NOT UP ANYMORE. DID I MISS SOMETHING?

DR. FISCHER-COLBRIE: NO. I PULLED IT BACK. THANK YOU.

CHAIRMAN GOLDSTEIN: OKAY. SO JUDY.

DR. GASSON: SORRY. I WAS GOING TO GO

AFTER MARK.

I WANT TO ADD TO WHAT AL HAS JUST SAID AND TO FULLY ENDORSE WHAT YOU'VE ARTICULATED, LARRY. I THINK THAT THERE'S NO DOUBT THAT THIS IS GOING TO BE A CHALLENGING UNDERTAKING. BUT I THINK THAT WE HAVE A RESPONSIBILITY, BASED UPON THE VOTERS OF CALIFORNIA APPROVING PROP 14, TO AT LEAST BEGIN A PROCESS WHERE WE CAN START TO TRY TO UNDERSTAND THE GENETIC BASIS OF SOME OF THESE DISORDERS THROUGH MODELING, THROUGH THE DEVELOPMENT OF LARGE COHORTS.

I THINK IT ALSO PROVIDES US WITH AN OPPORTUNITY, IF WE LOOK AT WHERE THE DISPARATE BURDEN OF SOME OF THESE DISEASE FALLS, IT PROVIDES US WITH AN OPPORTUNITY TO INCORPORATE OUR AFFORDABILITY AND ACCESSIBILITY CHARGE, WHICH IS ALSO LAID OUT IN PROP 14, BY MAKING SURE THAT THE RESEARCH IS NOT DONE SOLELY, AS IT FREQUENTLY HAS BEEN IN THE PAST, USING POPULATIONS OF PRIMARILY EUROPEAN DESCENT, BUT TO LOOK MUCH MORE BROADLY ACROSS CALIFORNIA, WHICH, OF COURSE, SOUTHERN CALIFORNIA HAS THE MOST ETHNICALLY DIVERSE POPULATIONS IN THE COUNTRY. WE LOOK LIKE THE REST OF THE COUNTRY IS GOING TO LOOK EVENTUALLY.

SO FOR THOSE TWO REASONS, I'M VERY ENTHUSIASTIC ABOUT YOUR PROPOSAL. THANK YOU.

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CHAIRMAN GOLDSTEIN: THANK YOU, JUDY. FRED.

DR. FISHER: SO I'M JUST LEARNING ALL OF THE THINGS THAT GO INTO THE NEURO BUCKET, SO TO SPEAK. AND IT'S A MUCH BIGGER BUCKET THAN I EVER IMAGINED. AS I SAID ON A PRIOR CALL, WHEN YOU LOOK AT THE NUMBER OF INDICATIONS THAT ARE AVAILABLE TO US, WE ARE NOT TALKING ABOUT A LOT OF MONEY, PARTICULARLY GIVEN THE DATA THAT WAS JUST PROVIDED WHERE IF IT'S GOING TO COST 1 TO 2 BILLION TO DEVELOP A DRUG AND THAT'S BEFORE YOU LOAD IN ALL THE OTHER COSTS THAT PHARMA DOES WHEN THEY TALK ABOUT THIS STUFF. WE DON'T HAVE ENOUGH MONEY TO CURE ONE NEURODEGENERATIVE DISEASE.

SO IT RAISES -- AND THIS IS NOT SO MUCH, LARRY, ABOUT YOUR PROPOSAL IN TERMS OF SHOULD WE LOOK AT THIS THING FIRST OR CREATE A GROUP TO LOOK AT THIS THING FIRST. SORT OF ZOOMING OUT A LITTLE BIT, I'M STILL TRYING TO IMAGINE WHAT OUR PROCESS IS AND HOW WE WEIGHT OR BALANCE SORT OF THE FIELD'S READINESS TO PURSUE NEURO, EVERYTHING THAT IS NOW PART OF THAT DEFINITION. EACH OF THOSE INDICATIONS HAS A FIELD, AND EACH OF THOSE FIELDS HAS A DEGREE OF READINESS TO PURSUE STEM CELL AND GENE THERAPY. AND CIRM CAN CERTAINLY BE A CATALYST FOR EXPLORATION

INTO THOSE AREAS. BUT SOME OF THOSE SPACES MAY NOT BE READY. THERE MAY NOT BE THE DISEASE MODELING OR UNDERSTANDING OF THE MECHANISMS SUFFICIENT TO EVEN PURSUE GENE OR STEM CELL-BASED THERAPIES.

SO I'M WONDERING IF THERE'S ANY VALUE IN BUILDING THAT INTO THE CALCULUS AROUND HOW WE LOOK AT AND HOW WE PRIORITIZE THE DIFFERENT DISEASE GROUPS OR INVESTMENT OPPORTUNITIES BASED ON THE READINESS OF THAT DISEASE GROUP TO ACTUALLY PURSUE STEM CELL, GENE-BASED THERAPY DEVELOPMENT. HOPEFULLY THAT MADE A LITTLE SENSE.

CHAIRMAN GOLDSTEIN: YES, FRED. I THINK IT'S A VERY SENSIBLE COMMENT. IT'S A TOUGH AREA. IT'S GOING TO REQUIRE A LOT MORE MONEY THAN WE HAVE ON OUR OWN. AND SO WE'LL NEED TO FIGURE OUT COLLABORATIONS, OR WE'LL NEED TO FIGURE OUT WHAT CAN WE DO THAT WILL MAKE A DIFFERENCE THAT'S NOT BEING PURSUED BY A LOT OF OTHER GROUPS.

NOW, WE'RE GOING TO HAVE TO WRAP UP SOON, AND I DON'T WANT TO CUT ANYBODY OFF PREMATURELY. WE ALSO NEED SOME PUBLIC COMMENT. SO LET ME PROPOSE THE FOLLOWING. THIS IS AN EXTREMELY IMPORTANT CONVERSATION. I SUGGEST THAT WE PURSUE IT AT THE BEGINNING OF THE NEXT MEETING, BUT ALSO THAT IN THE INTERIM I ARRANGE FOR A COUPLE OF GUEST EXPERTS WHO

WORK IN THIS AREA TO COME IN AND EDUCATE US A BIT ABOUT WHERE THINGS STAND AND WHERE WE MIGHT MAKE A DIFFERENCE. SO IF THERE IS NO MAJOR OBJECTION TO PROCEEDING IN THAT WAY, I'D LIKE TO TURN US TO PUBLIC COMMENT AND THEN TO ADJOURNMENT.

SEEING NO MAJOR OBJECTION, THAT'S GOOD.

MS. DEQUINA-VILLABLANCA: I DON'T SEE ANY, LARRY.

CHAIRMAN GOLDSTEIN: ANYTHING ON PUBLIC COMMENT, MARIANNE? OR IS THAT THE QUESTION YOU'RE ANSWERING?

MS. DEQUINA-VILLABLANCA: I DON'T SEE ANY PUBLIC COMMENT.

CHAIRMAN GOLDSTEIN: NO PUBLIC COMMENT. OKAY. SO WE HAVE ONE MINUTE UNTIL WE SHOULD BE ADJOURNING. SO WE'LL BEGIN OUR NEXT MEETING WITH A GENERAL DISCUSSION CONTINUING THIS TOPIC, BUT I WILL ALSO ARRANGE FOR A COUPLE OF EXPERTS IN AND AROUND THIS AREA OF NEUROPSYCHIATRIC TO COME IN AND EDUCATE US A BIT.

SO I THINK WITH THAT, WE ARE ADJOURNED.

(THE MEETING WAS THEN CONCLUDED AT 1:30 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 TASK FORCE ON NEUROSCIENCE AND MEDICINE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON FEBRUARY 21, 2021, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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