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: JUNE 20, 2023
2 P.M.

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

FILE NO.: 2023-22

I N D E X

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JUNE 20, 2023; 2 P.M.

(THE MEETING WAS DULY CALLED TO ORDER AND HEARD AS FOLLOWS:)

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

VICE CHAIR BONNEVILLE: PRESENT.

MS. DEQUINA-VILLABLANCA: MARK FISCHER-COLBRIE.

MR. FISCHER-COLBRIE: HERE.

MS. DEQUINA-VILLABLANCA: FRED FISHER. JUDY GASSON.

DR. GASSON: HERE.

MS. DEQUINA-VILLABLANCA: LARRY GOLDSTEIN.

CHAIRMAN THOMAS: HERE.

MS. DEQUINA-VILLABLANCA: DAVID HIGGINS.

DR. HIGGINS: HERE.

MS. DEQUINA-VILLABLANCA: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: HERE.

MS. DEQUINA-VILLABLANCA: STEVE JUELSGAARD.

MR. JUELSGAARD: PRESENT.

MS. DEQUINA-VILLABLANCA: PAT LEVITT.

DR. LEVITT: HERE.

MS. DEQUINA-VILLABLANCA: LAUREN MILLER-ROGEN.

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MS. MILLER-ROGEN: HERE.

MS. DEQUINA-VILLABLANCA: MARVIN SOUTHARD.

DR. SOUTHARD: PRESENT.

MS. DEQUINA-VILLABLANCA: KEITH YAMAMOTO.

OKAY. WE DO HAVE A QUORUM AND WE CAN PROCEED, LARRY.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU VERY MUCH.

SO TODAY'S MEETING WILL PRIMARILY BE FOCUSED ON ASKING QUESTIONS ABOUT THE CIRM PORTFOLIO AND THE DEGREE TO WHICH WE WANT TO DO PLANNING OF THAT PORTFOLIO. SO THE FIRST HOUR OR SO WILL BE A DEEPER DIVE INTO CIRM'S PAST FUNDING BEHAVIOR THAT'S BEEN PUT TOGETHER BY THE CIRM TEAM. THOSE OF YOU WHO HAVE HAD A CHANCE TO GLANCE AT IT KNOW THAT IT'S A PRETTY IMPRESSIVE DIVE AND PROVIDES A LOT OF INTERESTING INFORMATION.

AND THEN THE SECOND HOUR, I GUESS WHAT I'D LIKE TO TALK ABOUT IS IF THERE'S A BILLION AND A HALF SET-ASIDE, JUST AS AN ARGUMENT FOR THE AMOUNT, WHAT FRACTION OF THAT DO WE WANT TO PROGRAM BY ACTION OF THE BOARD AND THE CIRM TEAM TOGETHER VERSUS CONTINUING TO ALLOW THE GRANTS WORKING GROUP TO MAKE DECISIONS BASED ON PRIORITY AS APPLICATIONS COME IN FOR BROAD RFA'S. THIS IS A QUESTION ANY

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FUNDING AGENCY FACES, HOW MUCH CENTRALIZED PLANNING VERSUS HOW MUCH DISTRIBUTED REVIEW AND PRIORITY SETTING BY GRANT REVIEW.

SO TWO SORTS OF PITHY ISSUES TO GET US THROUGH THE DAY. AND SO LET'S GO TO THE ANALYSIS OF THE CIRM PORTFOLIO. WHO'S GOING TO PRESENT THAT?

DR. CANET-AVILES: I WILL PRESENT, DR. GOLDSTEIN, ON BEHALF OF THE CIRM TEAM REPRESENTED BY DR. CREASEY'S TEAM AND MY TEAM.

CHAIRMAN GOLDSTEIN: THANK YOU.

DR. CANET-AVILES: SO, MARIANNE, IF YOU WOULD LIKE TO PUT THE SLIDES UP PLEASE. THANK YOU. SO GO TO THE NEXT SLIDE.

AS DR. GOLDSTEIN WAS SAYING, THIS PRESENTATION IS A DEEP ANALYSIS AND GAP ANALYSIS OF OUR PORTFOLIO, AND THIS IS ALWAYS IN THE CONTEXT OF CIRM'S -- ACHIEVING CIRM'S MISSION TO ACCELERATE WORLD-CLASS SCIENCE TO DELIVER TRANSFORMATIVE REGENERATIVE MEDICINE TREATMENTS IN AN EQUITABLE MANNER TO A DIVERSE CALIFORNIA AND THE WORLD. NEXT SLIDE, MARIANNE.

SO THESE ARE THE QUESTIONS THAT MANY OF YOU ARE FAMILIAR WITH THAT WE ARE GOING TO BE ANSWERING. SO I'M GOING TO JUST GO THROUGH THEM VERY QUICKLY HERE. AND THEN BEFORE EVERY ANALYSIS,

WE WILL PLACE THE QUESTION. SO WE ARE GOING TO GO OVER WHAT IS THE PERCENTAGE OF DISC, TRAN, AND CLIN AWARDS THAT ARE WITHIN THE NEURO PORTFOLIO FROM 2007 TO 2023. SO THAT COULD INCLUDE PROP 14 AND 71, BUT WE ALSO DID A SOUP ANALYSIS THAT SHOWS JUST PROP 71 FROM ONE SIDE AND JUST PROPOSITION 14 SO THAT WE CAN SEE WHERE THERE ARE DIFFERENCES SINCE WE STARTED FUNDING.

THE PERCENT OF NEURO DISC AWARDS THAT HAVE PROGRESSED TO TRAN OR CLIN, WHAT'S THE PROGRESSION THAT WE GET FROM OUR EARLY FUNDING?

WHAT IS THE PERCENTAGE OF THESE AWARDS THAT ARE NEURO RELATIVE TO DISEASE BURDEN? AND WE DID THE SAME FOR TRAN AND CLIN.

AND THEN WE ARE GOING TO LOOK AT THE DISTRIBUTION OF NEURO AWARDS RELATIVE TO GEOGRAPHIC -- THE GEOGRAPHY OF OUR ACADEMIC AND MEDICAL RESEARCH INSTITUTIONS.

SO FOR THE FIRST QUESTION -- NEXT SLIDE, MARIANNE -- THE PERCENTAGE OF THESE TRAN AND CLIN AWARDS THAT ARE NEURO. NEXT. THIS IS FOR PROP 14 ONLY WHICH CORRESPONDS TO THE LAST NEARLY TWO YEARS. NEXT SLIDE.

WHAT WE CAN SEE IN THIS SLIDE IS THAT 37 PERCENT OF THE DISCOVERY AWARDS FOR PROP 14 HAVE

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CORRESPONDED TO NEURO AWARDS. AND THAT CORRESPONDS TO 34 AWARDS, AS YOU CAN SEE ON THE LITTLE TABLE ON THE RIGHT, OUT OF A TOTAL OF 91.

THE SECOND BAR CORRESPONDS TO TRANSLATIONAL. THE 27 AWARDS CORRESPONDING TO 9 TOTAL AWARDS OUT OF THE 33 CORRESPOND TO NEURO. AND THEN FOR CLINICAL IT'S 27 PERCENT AS WELL, WHICH IS 10 AWARDS OUT OF 37.

IF YOU WANT TO GO TO THE NEXT SLIDE, THIS IS FOR PROP 14. SO WE ARE GOING TO SEE WHETHER THIS IS CIRM -- THIS IS SUPPOSED TO BE -- THAT'S IN FUNDS. SORRY. AND THE LAST SLIDE WAS THE NUMBER OF AWARDS, AND THIS IS THE PERCENTAGE OF FUNDS. SO THE TOP OF THE GRAPH SAYS PERCENTAGE OF TOTAL AWARDS. IT'S ACTUALLY THE PERCENTAGE OF FUNDS THAT WE HAVE SPENT IN DISC, TRAN, AND CLIN IN PROP 14. SO THIS IS 57 PERCENT OF THE FUNDING. SO $50 MILLION THAT WE HAVE SPENT SO FAR IN NEURO. TRAN IS 26 PERCENT OF FUNDING, $39 MILLION. AND CLIN, 28 PERCENT, WHICH IS $86 MILLION.

AND NOW WE'RE GOING TO SEE THE PROP 71 ANALYSIS. NEXT SLIDE. THIS ACTUALLY IS THE TOTAL. WHAT WE WANT TO SEE HERE IS WHETHER THERE'S BEEN MUCH OF A DIFFERENCE BETWEEN WHAT WE'VE BEEN DOING SINCE WE RESTARTED PROP 14 AND WHAT WE HAVE DONE SO

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FAR. AND THE OVERALL CONCLUSION, IF YOU COMPARE THIS SLIDE TO THE ONE THAT WAS THE NUMBER OF AWARDS, IS THAT THERE IS NOT MUCH DIFFERENCE IN THE WAY WE ARE FUNDING NOW TO WHAT WE WERE FUNDING BEFORE. SO WE ARE DOING ABOUT THE SAME AMOUNT OF AWARDS. SO 28 PERCENT OF AWARDS, 196 TOTAL AWARDS WERE CORRESPONDING TO DISCOVERY; FOR TRANSLATIONAL, 53 OF THE AWARDS, WHICH IS ACTUALLY 34 PERCENT; AND FOR CLIN WAS 22 PERCENT, 30 AWARDS THAT CORRESPONDED TO NEURO. IT'S A LITTLE BIT MORE TRAN IN THIS CASE THAN WHAT WE ARE DOING NOW, BUT I WILL LEAVE THAT. I THINK THAT'S CONSIDERED MORE OR LESS THE SAME.

THE NEXT ONE IS GOING TO BE HOW MUCH MONEY HAVE WE SPENT, HOW MUCH FUNDING HAVE WE SPENT IN PROP 71 AND PROP 14 FOR NEURO. NEXT SLIDE.

IN TERMS OF FUNDING, WE HAVE SPENT $362 MILLION IN DISCOVERY IN NEURO. THAT'S ABOUT 31 PERCENT OF THE FUNDING. 35 PERCENT OF FUNDING, $204 MILLION FOR TRAN. AND 29 PERCENT FOR CLIN OR $367 MILLION THAT WE SPENT. SO, AS YOU CAN SEE, WE SPENT ABOUT THE SAME AMOUNT FOR TRAN AND CLIN IN NEURO IN THE PAST.

ANY QUESTIONS SO FAR? AND THEN IF WE WANT TO TAKE QUESTIONS NOW, PERHAPS AT THE END, DR. GOLDSTEIN.

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CHAIRMAN GOLDSTEIN: WE SHOULD TAKE QUESTIONS AT THE END. LET ME JUST INTERJECT ONE POINT. IF YOU ASK WHAT FRACTION OF 5.5 BILLION IS THE 1.5 BILLION SET-ASIDE, THE ANSWER IS 27 PERCENT. SO THE NUMBERS YOU ARE SEEING THAT ARE GREATER THAN 27 PERCENT, WHICH IS MOST OF THEM, THAT ACTUALLY IN A SENSE REFLECTS HAVING COMPLETELY FULFILLED THE MISSION SO FAR JUST BY DOING NOTHING OTHER THAN BROAD RFA'S AND SELECTING THE BEST PROPOSALS BASED ON THAT.

SORRY, ROSA. GO AHEAD.

DR. CANET-AVILES: THANK YOU. NO. NO. NO. THAT WAS A GREAT COMMENT. THANK YOU, DR. GOLDSTEIN.

SO NOW WHAT WE ARE GOING TO LOOK AT IS THE PROGRESSION OF THE FUNDING FROM DISCOVERY. WHAT IS THAT WE BASICALLY DERISK TO GO INTO TRAN AND CLIN PROGRESSION. SO NEXT SLIDE.

WE CAN SEE THAT THERE ARE 28 PROJECTS THAT PROGRESSED IN TOTAL, IN THE TOTAL PORTFOLIO OF CIRM FROM SOME STAGE TO TRAN OR CLIN IN TOTAL. OF THOSE 28, 15 OF THEM WENT FROM DISCOVERY TO TRAN AND CLIN. AND YOU CAN SEE THEM AS THE DISCOVERY WOULD BE THE GREEN BOXES. AND OF THOSE THERE ARE 15 THAT GO EITHER FROM DISCOVERY IDEA, DISCOVERY CANDIDATE TO

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TRAN OR TO CLIN OR TO TRAN AND CLIN. SO OF THOSE WE COUNT UP THE RISK INTERNALLY, 15 OF THEM. AND THAT CORRESPONDS TO 2 PERCENT OF THE TOTAL DISCOVERY AWARDS; I.E., 689 AWARDS. THAT'S THE TOTAL OF DISCOVERY AWARDS. SO 2 PERCENT IS THE 15.

AND THE COLOR CODING IS THE INDICATION. SO THE HIGHEST NUMBER THAT WE HAVE SEEN IN TERMS OF PROGRESSION HAS BEEN NEURODEGENERATION, PARKINSON'S, ALS, HUNTINGTON'S. AND THEN WE HAVE A FEW IN EYE, AS INDICATED BY THE RETINITIS PIGMENTOSA AND MACULAR DEGENERATION AWARD, BUT THAT'S FROM TRAN TO CLIN. IT'S NOT FROM DISCOVERY. AND THEN WE HAVE SOME IN SPINAL CORD INJURY AND ONE IN TRAUMATIC BRAIN INJURY. AND THEN WE HAVE TWO IN EPILEPSY AND THEN -- WE HAVE ACTUALLY ONLY ONE IN EPILEPSY THAT WENT FROM EARLY DISCOVERY IDEA TO CANDIDATE TO CLIN1 AND CLIN2 DIRECTLY. IT KIND OF BYPASSED THE TRAN. AND THAT'S ACTUALLY A COLLABORATION WITH A COMPANY BETWEEN ACADEMIA AND THEN COMPANIES NEURONA THERAPEUTICS.

AND THEN WE HAVE ONE THAT'S IN CANAVAN DISEASE THAT WENT FROM DISCOVERY CANDIDATE TO TRANSLATIONAL.

SO THE NEXT SLIDE IS GOING TO SHOW US THE PERCENTAGE OF DISC AWARDS THAT ARE NEURO RELATIVE TO

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DISEASE BURDEN. SO HOW MUCH AND THEN WE DID THE SAME FOR THE PERCENTAGE OF TRAN AND CLIN AWARDS RELATIVE TO DISEASE BURDEN IN THE POPULATION. SO WE ARE GOING TO SEE HOW MUCH HAVE WE FUNDED.

DISEASE BURDEN, WE CALCULATED -- IS REPRESENTED HERE BY THE DALY, WHICH IS DISABILITY ADJUSTED LIFE YEAR, WHICH IS A PRESENTATION OF THE LOSS EQUIVALENT OF ONE YEAR OF FULL HEALTH. AND THESE NUMBERS ARE UP TO DATE, AND THEY INCLUDE GLOBAL HEALTH AND WHO NUMBERS.

SO THE CIRM FUNDING FOR DISCOVERY HERE, WE HAD THE HIGHER FUNDING WAS IN PARKINSON'S DISEASE WITH $51 MILLION GOING INTO NEUROTRAUMA, ALS, EYE DISEASES, ALZHEIMER'S, AND THEN GOING DOWN -- WHAT HAPPENED? IS IT ME OR --

MR. JUELSGAARD: NO. IT'S THE PRESENTATION.

DR. CANET-AVILES: OKAY. GOT IT. BECAUSE I'M ACTUALLY IN A NON-IDEAL SETTING, SO I WASN'T SURE. THANK YOU, MR. JUELSGAARD.

SO THAT'S WHAT WE WERE LOOKING AT. AND THEN, AS YOU CAN SEE, IF YOU MAP THESE TO THE DALY, WE CAN SEE THAT FOR PARKINSON'S DISEASE, THE DISEASE BURDEN IS RELATIVELY LOWER THAN, SAY, STROKE, AS I SAID, AS REPRESENTED BY THE LOSS OF EQUIVALENT OF

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ONE YEAR OF FULL HEALTH. BUT THEN WE CAN SEE THAT WE HAVE VERY LITTLE FUNDING FOR SOME DISEASES THAT HAVE A VERY STRONG BURDEN, AS YOU CAN SEE, FOR EXAMPLE, AT THE BOTTOM WITH NEUROPSYCHIATRIC DISEASES AND THEIR BURDEN.

NEXT SLIDE IS GOING TO SHOW THE DISEASE BURDEN FOR TRAN AND CLIN AWARDS. SO FOR TRAN WE CAN SEE -- NEXT SLIDE, MARIANNE. FOR TRAN YOU CAN SEE THAT THE HIGHEST AMOUNT OF FUNDING WAS FOR BRAIN CANCER AND EYE DISORDERS FOLLOWED BY ALZHEIMER'S DISEASE AND STROKE AND OTHER NEURODEVELOPMENTAL DISORDERS. AND THEN WE HAVE TRAUMA AND HUNTINGTON'S DISEASE, EPILEPSY. BUT, AGAIN, WE HAVE A RELATIVELY GOOD AMOUNT OF FUNDING IN DISEASES THAT HAVE A LOWER DALY BURDEN; BUT THEN FOR THOSE THAT HAVE HIGHEST, LIKE, FOR EXAMPLE, AUTISM SPECTRUM DISORDERS, WE HAVE NOTHING, IT'S NOT AS HIGH A BURDEN, BUT THEN, AGAIN, NEUROPSYCHIATRIC LOOKS VERY LOW, VERY SMALL.

THE NEXT ONE -- AND THAT'S ALSO PROBABLY BECAUSE OF THE STATE OF THE SCIENCE AT THE TIME AS WELL, RIGHT. AND FOR TRANSLATIONAL AND CLINICAL NEUROPSYCHIATRIC, THERE MIGHT NOT BE MUCH THAT WE CAN DO. HOWEVER, WE MAY BE ABLE TO DO MORE TOWARD DISCOVERY AS WE'VE ALREADY DISCUSSED.

NEXT SLIDE IS FOR CLIN. AND HERE AGAIN WE

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HAVE A BIT OF A SWITCH FROM DISCOVERY IN WHICH BRAIN CANCER AND EYE DISORDERS AS WELL AS SOME NEURODEGENERATIVE DISORDERS LIKE ALS AND NEUROTRAUMA AND STROKE ARE LIKE THE HIGHEST FUNDING. AND, AGAIN, WE CAN SEE THAT THERE IS A LOW LEVEL OF FUNDING. SURPRISINGLY FOR ALZHEIMER'S DISEASE, THERE'S BEEN DISCOVERY AND TRANSLATIONAL, BUT THERE IS NOTHING HERE IN THE CLINICAL. BUT OBVIOUSLY THERE IS, IN TERMS OF CELL THERAPIES OR GENE THERAPIES, WE STILL DON'T HAVE ANYTHING FOR ALZHEIMER'S DISEASE. SO I'M NOT SURPRISED HERE. IT'S MORE SMALL MOLECULES. NEXT SLIDE. AND IMMUNOTHERAPIES.

NOW WE'RE GOING TO SEE THE DISTRIBUTION OF NEURO AWARDS RELATIVE TO THE GEOGRAPHY OF ACADEMIC AND MEDICAL RESEARCH INSTITUTIONS. SO FOR DISCOVERY WE CAN SEE THAT THE HIGHEST AMOUNT OF FUNDING, THE HIGHEST NUMBER OF AWARDS IS ACTUALLY IN THE SOUTH, IN THE SAN DIEGO AREA, FOLLOWED BY THE SAN FRANCISCO BAY AREA AND THEN LOS ANGELES AND ORANGE COUNTY. THE SHASTA/SACRAMENTO AREA HAS ABOUT FOUR FOLLOWED BY CENTRAL COAST AND THE INLAND EMPIRE, AND OUTSIDE OF CALIFORNIA THERE IS ONE AWARD.

THE NEXT SLIDE SHOWS FOR THE TRAN AWARDS. THE BAY AREA IS THE ONE THAT HAS THE HIGHEST NUMBER

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OF AWARDS FOLLOWED BY SAN DIEGO, LOS ANGELES, AND ORANGE COUNTY, AND THEN AGAIN, SHASTA/SACRAMENTO WITH THE CENTRAL COAST AND THE INLAND EMPIRE THAT DON'T HAVE AS MANY AWARDS.

AND THEN THE NEXT SLIDE IS THE CLINICAL NUMBER OF AWARDS. LOS ANGELES AREA IS THE ONE THAT HAS THE HIGHEST CLINICAL NEURO AWARD NUMBER IN CALIFORNIA FOLLOWED BY THE BAY AREA AND ORANGE COUNTY, THE SHASTA/SACRAMENTO, AND THEN OUTSIDE CALIFORNIA THERE ARE TWO AWARDS, AND SAN DIEGO AREA HAS TWO AWARDS.

AND THEN I THINK NOW WE ARE GOING TO GO INTO THE QUESTIONS, BUT I THINK DR. GOLDSTEIN ALREADY -- MARIANNE, YOU WANT TO MOVE THE SLIDES TO THE NEXT. RIGHT.

SO THE THREE QUESTIONS I THINK I'M GOING TO LEAVE IT TO YOU, DR. GOLDSTEIN.

CHAIRMAN GOLDSTEIN: YEAH. LET'S HOLD OFF ON THESE -- THANK YOU, ROSA. LET'S HOLD ON THESE FOR THE TIME BEING.

SO, FIRST OF ALL, THANK YOU, ROSA, FOR THE GREAT PRESENTATION AND THANK YOU TO ALL THE DIFFERENT MEMBERS OF THE CIRM STAFF WHO PULLED THESE NUMBERS TOGETHER. THIS WAS A GOOD, SOLID ANALYSIS OF THE DATA THAT WE CURRENTLY HAVE AND THAT ACTUALLY

POSE SOME INTERESTING QUESTIONS.

SO FIRST OFF, QUESTIONS ABOUT THE DATA THEMSELVES FROM THE GROUP PLEASE. MARK.

MR. FISCHER-COLBRIE: TERRIFIC DATA, WELL SUMMARIZED. DATA ALWAYS GENERATES ADDITIONAL QUESTIONS. THE NEURO PROGRESSION SLIDE WAS REALLY INTERESTING TO ME IN THE CONTEXT OF I'D BE REALLY INTRIGUED ABOUT WHETHER SOME OF THOSE THINGS THAT ARE ON THAT PROGRESSION SLIDE HAS FURTHER OPPORTUNITIES FOR FUTURE PROGRESSION OR IF THINGS COME TO A HALT. AND IF THEY HAVE COME TO A HALT, IS IT BECAUSE THE SCIENTIFIC ADVANCEMENT IS NOT POSSIBLE OR IS IT RELATED TO FUNDING?

SO I DON'T KNOW IF THERE'S A WAY WITHOUT EXPENDING AN INORDINATE AMOUNT OF TIME TO UNDERSTAND THAT BECAUSE OBVIOUSLY WITHIN OUR CONTEXT WE ARE TRYING TO MOVE THINGS FORWARD ON A CONTINUOUS BASIS FROM START TO FINISH. IT WOULD BE REALLY INTERESTING TO SEE IF THERE'S STILL OPPORTUNITIES FOR SOME OF THOSE ON THE PROGRESSION SLIDE TO CONTINUE FORWARD.

CHAIRMAN GOLDSTEIN: I WOULD JUST ADD, MARK, IT'S A GOOD POINT BECAUSE WE DON'T HAVE DATA COMPILED YET ON PROJECTS THAT WENT, SAY, FROM DISC INTO PRIVATE INDUSTRY OR THAT TRAVELED WITH PEOPLE

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WHO LEFT THE LAB TO GO SOMEWHERE ELSE. WE HAVE A DRUG CANDIDATE THAT EMERGED THAT WENT WITH AN EX POST-DOC OF MINE TO THE NETHERLANDS, WHICH IS WHERE THE TRIALS ARE GOING TO BE. SO IT'S NOT THAT THINGS DON'T PROGRESS MEDICALLY OR SCIENTIFICALLY NECESSARILY. SOMETIMES WE JUST DON'T KNOW WHERE THEY WENT.

STEVE.

MR. JUELSGAARD: YES. I'M STRUCK ON SLIDE 13 WHICH SHOWS THE NEURO PROGRESSION BY DISEASE AREA. WHAT WE LISTED IN THE SECOND COLUMN ARE ALL INSTITUTIONS. AND I DON'T SEE ANY INDUSTRY INVOLVEMENT IN ANY OF THESE PARTICULAR AREAS, AND YET WE'VE BEEN FUNDING INDUSTRY IN A NUMBER OF AREAS. SO IS IT THAT INDUSTRY IS JUST NOT ASKING FOR MONEY FROM CIRM FOR THE NEUROLOGICAL AREA, OR WHAT DO YOU THINK THE ISSUE IS THAT WE ARE ONLY SEEING INSTITUTIONAL INVOLVEMENT? THERE, THAT'S THE SLIDE. SECOND COLUMN OVER, INSTITUTION.

DR. CANET-AVILES: SO THERE IS -- ONE OF THE QUESTIONS THAT WAS FLOATED WAS HOW MUCH OF THIS PORTFOLIO HAS BEEN DERISKED THAT HAS GONE FROM, SAY, DISCOVERY INTO TRANSLATIONAL OR CLINICAL BUT OUTSIDE LIKE, SAY, INDUSTRY. AND I DON'T KNOW IF OUR COLLEAGUE FROM BUSINESS DEVELOPMENT, DR. SHYAM

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PATEL, IS ON THE LINE AND WHETHER WE HAVE DATA ON THIS. BUT I COULD SAY -- IS HE THERE? I DON'T KNOW IF HE'S THERE. HE'S NOT.

OKAY. WE CAN ACTUALLY GET BACK TO YOU ON THIS. MY FIRST -- MY SUSPICION IS THAT THERE IS VERY LITTLE BECAUSE WE WOULD HAVE RECORDED THAT. SO I THINK THE AREAS, THE KIND OF FUNDING THAT WE HAVE DERISKED MOSTLY HAS BEEN GOING TO ACADEMIC INSTITUTIONS AS SHOWN IN THIS SLIDE. AND WE WILL GET YOU THE NUMBERS IF THERE ARE ANY OUTSIDE THE DERISKING.

MR. JUELSGAARD: JUST A FOLLOW-UP QUESTION, ROSA. AND IT MAY BE ACTUALLY FOR SOMEBODY ELSE IN THE ROOM. IF I GO BACK TO WHAT I CALL THE OLD DAYS, LET'S SAY I LOOK BACK AT 2016 AND THE GRANTS WE WERE MAKING IN THOSE DAYS. THE GRANTS THAT WERE BEING MADE WERE ACTUALLY IN EXCESS OF THE GRANT LIMIT. SO, FOR EXAMPLE, WE MIGHT HAVE A TRANSLATIONAL LIMIT BACK IN THOSE DAYS OF $5 MILLION, AND YET A GRANT WAS MADE IN THE NEIGHBORHOOD OF $7.6 MILLION. AND WHILE I DON'T RECALL FOR SURE, I ASSUME THAT THE DIFFERENCE WAS THE OVERHEAD PART ASSOCIATED WITH AN ACADEMIC INSTITUTION THAT DROVE THE AMOUNT OF MONEY UP, IN THIS CASE FROM, SAY, 5 TO 7.5 OR 7.6 MILLION.

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IS THAT THE WAY WE ARE STILL PROVIDING SUPPORT IS WE HAVE A STANDARD GRANT AMOUNT, BUT THEN SORT OF IN THE BACKGROUND THERE'S THE ADMINISTRATIVE SUPPORT OR OVERHEAD COMPONENT WHICH REALLY ISN'T IN THE NUMBERS THAT WE APPROVE? DOES ANYBODY KNOW THAT?

DR. CREASEY: YES. THE TRAN GRANTS AND CLIN GRANTS INCLUDE THE OVERHEAD JUST LIKE -- I'VE BEEN WITH CIRM SINCE 2016. AND WHAT YOU JUST DESCRIBED, MR. JUELSGAARD, IS INCLUDED. SO NOTHING HAS CHANGED.

MR. JUELSGAARD: WELL, IF YOU, FOR EXAMPLE, GO BACK TO -- IF I LOOK AT WHAT WAS DONE, WHAT DATE WAS THIS, ON MARCH 16TH OF 2016 AND YOU LOOK AT THE AWARDS THAT WERE BEING MADE AND JUST LOOK AT THAT IN PARTICULAR. BRING UP THE SUMMARIES FOR A MOMENT. THE ONE THAT GOT THE HIGHEST SCORE, WHICH WAS 95, THE BUDGET AMOUNT THAT WAS APPROVED WAS $7.377 MILLION. THERE WAS ANOTHER ONE THAT SCORED 85 THAT GOT $7.659 MILLION. AND YET THE SLIDES FOR THAT PRESENTATION SHOWED THE MAXIMUM AMOUNT FOR THIS TRAN AWARD OF BEING, IN THOSE DAYS, $5 MILLION. SO I'M JUST TRYING TO MAKE SENSE OF WHAT WE DID BACK THEN AND WHETHER WE ARE DOING THE SAME THING TODAY.

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DR. MILLAN: WE HAVE JENN LEWIS HERE WHO IS HEAD OF GRANTS MANAGEMENT. I'M GOING TO REPEAT THE QUESTION.

MS. LEWIS: I HEARD IT. SO, STEVE, I THINK YOU'RE RIGHT. SO I THINK THE DIFFERENCE IS IN TRANSLATION. YOU'RE CORRECT THAT IN OUR TRANSLATION PROGRAM WE HAVE A TOTAL CAP ON OUR DIRECT COST AMOUNT, AND THEN ON TOP OF THAT AWARDEES CAN ASK FOR ANY ELIGIBLE OVERHEAD. SO THAT'S WHY YOU MIGHT SEE A VARIANCE BETWEEN THE NUMBERS.

IN CLIN THAT IS THE ONLY PROGRAM WHERE WE HAVE A TOTAL AWARD CAP. SO OVERHEAD IS INCLUDED IN THAT TOTAL AWARD CAP.

MR. JUELSGAARD: GOT IT. SO THESE DAYS WHEN WE APPROVE TRAN AWARDS, WE DON'T SEE THAT OVERHEAD AMOUNT SHOWN IN THE AWARDS WE APPROVE. WE ARE JUST SEEING THE BASE AMOUNT?

MS. LEWIS: NO. YOU'LL SEE -- THE TOTAL AWARD AMOUNT WILL INCLUDE BOTH THE DIRECT AND THE OVERHEAD AMOUNT WHEN YOU'RE APPROVING THOSE GRANTS.

MR. JUELSGAARD: HUH. OKAY. I DON'T RECALL SEEING THAT.

ANYWAY, ONE OF THE POINTS I WANTED TO MAKE WAS IS THAT, WHEN I LOOK BACK AT WHAT WAS HAPPENING WAY BACK IN 2016, AND I WANT TO REMIND PEOPLE THAT

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COSTS WERE A LOT LOWER IN 2016 THAN THEY ARE NOW IN 2023 IN ALL SORTS OF AREAS, BUT THAT INCLUDES THE AREA OF RESEARCH AND CLINICAL DEVELOPMENT. SOME OF THE MOST -- THE GRANTS WITH THE GREATEST AMOUNTS OF MONEY WERE ACTUALLY IN THE NEUROLOGICAL AREA. SO THERE WAS A BIGGER ASK FOR GRANTS THAT INVOLVE DISEASES INVOLVED WITH THAT ISSUE.

AND IT BRINGS ME BACK AROUND TO A DISCUSSION THAT WE HAD EARLIER WHEN I -- FORGET THE RESEARCHER FROM STANFORD -- BUT WE ASKED WHY HE HADN'T APPLIED FOR RESEARCH GRANTS FROM CIRM. AND HE SAID, "WELL, IT'S JUST NOT WORTH TAKING THE TIME TO DO IT BECAUSE THE AMOUNT OF MONEY THAT'S INVOLVED IS JUST NOT ADEQUATE FOR THE KIND OF WORK THAT I NEED TO DO." AND I'VE BEEN TRYING TO FIGURE OUT KIND OF WHERE WE'VE BEEN AND WHAT WE'VE BEEN DOING IN THE MEANTIME. AND I HAVEN'T BEEN ABLE TO DO AS MUCH WORK AS I'D LIKE TO TO KIND OF LOOK BACK OVER TIME, BUT I'M NOT SURE WE HAVE CHANGED THE SIZE OF OUR GRANT AMOUNTS FROM MAYBE, LET'S SAY, 2016 TO TODAY BY ANY APPRECIABLE AMOUNT IF WE'VE EVEN INCREASED THEM AT ALL.

AND I THINK -- AND THIS MAY APPLY MORE GENERALLY THAN JUST TO THE NEUROLOGICAL AREA, BUT I THINK IT'S ONE OF THOSE THINGS THAT WE NEED TO HAVE

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A LOOK AT AS TO WHETHER OR NOT WE ARE KIND OF KEEPING UP WITH THE TIMES, SO TO SPEAK. I DO KNOW ON THE INDUSTRY SIDE FROM PERSONAL EXPERIENCE IN DEALING WITH PEOPLE IN INDUSTRY, THE COSTS CERTAINLY HAVE INCREASED FOR BOTH MATERIALS AND SUPPLIES, FOR LABOR. FOR CLINICAL RESEARCH ORGANIZATIONS, THERE HAVE BEEN SOME APPRECIABLE COST INCREASES IN THIS DAY AND AGE.

ANYWAY, I JUST HAD AN INTEREST IN AND HAD A QUESTION ABOUT IT IS WHETHER, AND IT GOES ALL BACK TO THE QUESTION OF WHETHER OR NOT WE ARE PROVIDING ADEQUATE FUNDING HERE IN THE NEURO AREA FOR ANY OF THESE DISEASES. IT'S SOMETHING I THINK WE NEED TO TAKE A GOOD LOOK AT IT. THANK YOU.

CHAIRMAN GOLDSTEIN: THANK YOU, STEVE. THAT'S ACTUALLY QUITE PERCEPTIVE.

DR. CANET-AVILES: CAN I --

CHAIRMAN GOLDSTEIN: LET ME JUST MAKE A COMMENT AND THEN, YES, ROSA, I'LL PASS IT ON TO YOU.

ONE THING TO BE THINKING ABOUT THROUGHOUT THIS CONVERSATION IS DO WE WANT OUR ALLOCATIONS OF FUNDING TO BE MATCHED TO DISEASE BURDEN, DISEASE FREQUENCY, DISEASE COST, DISEASE DISRUPTION OF PEOPLE'S LIVES? THIS IS, AGAIN, A STANDARD SET OF QUESTIONS THAT FUNDING AGENCIES COPE WITH.

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ROSA.

DR. CANET-AVILES: I WAS JUST GOING TO COMMENT AND CLARIFY THAT WE'VE BEEN HEARING THIS COMMENT, AND WE ARE AWARE, AND WE ARE WORKING ON THIS. AND AT LEAST FOR THE NEW CONCEPT THAT IS COMING IN SEPTEMBER, WE ARE TAKING THIS INTO ACCOUNT AT LEAST FOR THE NEURO STRATEGY THAT HAS TO DO WITH DISCOVERY. SO THE MODEL AND THE STRUCTURE THAT WE WOULD BE PRESENTING COULD BE REFLECTING THIS. JUST WANTED TO MAKE THAT COMMENT, THAT WE ARE HEARING IT LOUD AND CLEAR.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU. MARK.

MR. FISCHER-COLBRIE: MY QUESTION HAS TO DO WITH CIRM HAD TO CHOKE OFF A BUNCH OF FUNDING AS FUNDING WAS RUNNING DOWN, AND A LOT OF RESEARCHERS WERE DISCOURAGED FROM FILING APPLICATIONS. AND WHEN I WENT TO BACK TO REVISIT PEOPLE UPON JOINING CIRM, THEY HAD, INTERESTINGLY ENOUGH, THEY HAD BEEN PRIOR GRANT AWARDEES WERE WAY BEHIND THE TIMES ON WHERE CIRM WAS AT, WHAT THE STATUS WAS, WHAT WAS GOING ON WITH THE ADDITION OF CELL THERAPY, THE SIZE OF THE GRANTS, AND THE SEQUENCING. AND IT'S LIKE, OH, YOU GUYS ARE BACK OPEN FOR BUSINESS? THEY HAD NO ACKNOWLEDGEMENT. AND WE ARE TALKING, SURPRISINGLY,

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ABOUT SOME INDIVIDUALS AT UCSF AND STANFORD AND A LOT OF OTHER PLACES.

AND THE REASON FOR THAT INTRO, AND IT GETS BACK TO THE LAST QUESTION, I SUSPECT THERE'S A VAST AMOUNT OF MISINFORMATION RUNNING AROUND ABOUT DOLLAR AMOUNTS AND HOW HARD IT IS TO FILE AN APPLICATION BECAUSE FOR A WHILE RESEARCHERS WERE DISCOURAGED FROM FILING CERTAIN TYPES OF APPLICATIONS BECAUSE OF THE DWINDLING FUNDS AND, THEREFORE, WERE DIRECTED NOT TO DO THAT IN A WAY, IT'S NOT SCIENTIFIC TERMINOLOGY, BUT I BELIEVE THEY WERE DISCOURAGED.

SO THE COROLLARY QUESTION I HAVE, AGAIN GETTING BACK TO DISEASE PROGRESSION, IS THE PHENOMENON. DID WE CHOKE OFF ANY GRANTS THAT PEOPLE HAVE APPLIED FOR, BUT WE WERE OUT OF FUNDING OR WERE DWINDLING DOWN ON FUNDING OR FUNDING GOT REDIRECTED TO OTHER AREAS SO THEY'RE IN THE RESURRECTION, IF YOU WILL.

AND THIS IS GOING TO BE MY RUN-IN TO A THEMATIC ASPECT OF I THINK IT'S CRITICAL THAT WE ON A PROPER BASIS SET UP DIRECTED AREAS OF STUDY TO BRING A VAST ARRAY OF RESEARCHERS TOGETHER UNDER CONSORTIA TO ADVANCE THE CAUSE. AND THAT CAN BE DONE ON DEFINED AREAS AND WITH DEFINED DOLLAR AMOUNTS IN AGGREGATE. THAT WAS HIGHLY SUCCESSFUL

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DURING MY TENURE AT JUVENILE DIABETES RESEARCH FOUNDATION. ALL KINDS OF BREAKTHROUGHS AND THE FACT THAT PEOPLE WERE ABLE TO WORK ON A COLLABORATIVE BASIS ACROSS A LOT OF DIFFERENT INSTITUTIONS TO PIGGYBACK OFF RESEARCH WAS INCREDIBLY POWERFUL. BUT ONE OF THE BIGGEST ELEMENTS WAS A CENTRALIZED DATA STREAM OF INFORMATION THAT THEY OTHERWISE WOULDN'T HAVE HAD ACCESS TO.

SO ANYWAY, THAT'S ALL KIND OF BLENDED TOGETHER A BUNCH OF MISHMASH COMMENTS. SO MY APOLOGIES.

CHAIRMAN GOLDSTEIN: THANK YOU, MARK. ACTUALLY THAT WAS HELPFUL.

PAT.

DR. LEVITT: I HAVE A FEW COMMENTS. THE COMMENTS ABOUT THE SIZE OF THE GRANTS WAS MADE BY ONE OF THE PRESENTERS RELATED TO THE DISCOVERY GRANTS. THE PRESENTERS WERE NOT REALLY INVOLVED IN THE TRANS OR CLIN AREAS. AND IT'S GREAT TO HEAR THAT CIRM IS -- THAT THE TEAM IS CONSIDERING AND HEARING LOUD AND CLEAR WHAT'S GOING ON IN TERMS OF RESEARCH COSTS, WHICH IS WAY AHEAD OF THE NIH, WHICH IS STILL USING CAPS DEFINED BACK IN 1995 FOR THE SIZE OF BASIC RESEARCH GRANTS.

SO I THINK IT'S IMPORTANT TO CONSIDER THAT

BECAUSE THE EXPENSES, PARTICULARLY -- IT'S BAD ENOUGH ON THE SUPPLY SIDE, BUT THE PERSONNEL SIDE, THERE HAVE BEEN MAJOR CHANGES IN A VERY SHORT PERIOD OF TIME IN THE STATE OF CALIFORNIA WHERE NEARLY ALL OF THE GRANTS GO. SO WHAT USED TO COST -- THERE'S AT LEAST A 25-, 30-, SOMETIMES 40-PERCENT INCREASE IN SALARIES. SO THAT'S REALLY IMPORTANT.

THE OTHER IS THAT IN THE NEURO AREA, GIVEN WHAT WE HEARD IN THE PRESENTATIONS AND THE KIND OF MODELS, TO BE HONEST, I CAN'T REMEMBER WHAT THE AVERAGE LENGTH IS FOR AN AWARDED DISC GRANT. IS IT THREE YEARS? IS IT FIVE YEARS? IS IT FOUR YEARS? DOES IT VARY?

DR. CREASEY: THREE YEARS FOR TRAN.

DR. CANET-AVILES: DISC.

DR. CREASEY: DISC?

DR. CANET-AVILES: SO DISC IS TWO YEARS FOR DISC-0 AND THREE YEARS FOR DISC2.

DR. LEVITT: SO I WOULD SAY THAT'S A REAL PROBLEM, RIGHT, BECAUSE THREE YEARS, WHEN YOU'RE GROWING ORGANOIDS AND IT TAKES SIX TO NINE MONTHS TO GET YOUR FIRST ONES, RIGHT, THEY DON'T TAKE TWO WEEKS. YOU'RE NOT DOING MOUSE WORK. A THREE-YEAR PROJECT IS REALLY CHALLENGING TO PULL THIS OFF. SO WE HAVE TO THINK ABOUT THAT IN TERMS OF WHETHER

CERTAIN -- AND THAT CAN BE DONE THROUGH RFA'S -- CERTAIN AREAS OF EMPHASIS. HUMAN DISEASE MODELS IN PSYCHIATRY, FOR EXAMPLE, YOU CAN SEE THE NUMBER OF GRANTS ARE LIKE MINUSCULE. YOU JUST CAN'T DO IT IN THREE YEARS. SO SOME OF IT IS THE DOLLAR AMOUNT, BUT SOME OF IT ALSO IS THE LENGTH OF TIME AND WHETHER THE BRAIN TRUST WILL FEEL THAT DISTINGUISHING BETWEEN LENGTH OF TIME IS A REASONABLE PROCESS.

BUT I DON'T KNOW WHO CAN DO SOME OF THESE -- ANY OF THESE PROJECTS THAT WE HEARD ABOUT IN TWO OR THREE YEARS. I'LL STOP THERE.

DR. CANET-AVILES: SO FOR DISC2, FOR EXAMPLE, FOR THE DEVELOPMENT CANDIDATE, WE HAVE THREE YEARS, BUT THEY HAVE TO COME WITH PRELIMINARY DATA. I JUST WANTED TO CLARIFY THAT. SO THERE'S ENOUGH.

NOW FOR DISCOVERY, I COULD SAY WE ARE, AS I WAS MENTIONING, GOING TO BE PRESENTING A NEW CONCEPT FOR THE NEURO DISCOVERY STRATEGY THAT IS GOING TO TAKE INTO ACCOUNT THE TIME NEEDED TO INNOVATE RISKY PROJECTS AND THE TIME NEEDED TO COLLABORATE THEM. WE ARE GOING TO BE BRINGING THIS UP TO THE BOARD. SO WE ARE LISTENING. WE ARE TAKING INTO ACCOUNT ALL THESE DIFFERENT FACTORS, AND

WE ARE ALSO LOOKING AT WHAT OTHER SUCCESSFUL ORGANIZATIONS HAVE BEEN DOING, NOT JUST THE NIH, BUT OTHERS LIKE HHMI, ET CETERA. SO WE WILL BE TAKING THAT INTO ACCOUNT.

DR. LEVITT: I THINK THAT'S GREAT. AND I THINK THAT WILL STIMULATE A LOT MORE ACTIVITY IF SOME MODIFICATIONS ARE MADE. TO BE HONEST, PREPANDEMIC YOU WERE LIKELY MORE READY TO RUN ON A PROJECT ONCE IT GOT FUNDED BECAUSE YOU HAD FOLKS IN THE RESEARCH GROUP THAT WERE ALREADY TRAINED. FILLING STAFF POSITIONS IS FAR MORE DIFFICULT NOW. TRAINING TAKES MORE TIME. THESE ARE ALL THE THINGS THAT ARE HAPPENING IN THE FIRST YEAR. YOU CAN'T START THAT UNTIL YOU GET THE GRANT. SO I'M JUST SAYING THAT IT'S MORE THAN JUST THE COST OF THE SALARY COST OR THE RESOURCES, MATERIALS AND SUPPLIES. IT'S ALSO THESE OTHER LOGISTICS THAT ARE EXTREMELY DIFFICULT NOW.

SO WHATEVER YOU CAN DO TO ADAPT IN A WAY THAT'S REALLY PROACTIVE, I THINK THAT'S GREAT. IT WILL TAKE NIH A LOT LONGER TO DO IT. SOME OF US HAVE HAD CONVERSATIONS WITH INSTITUTE DIRECTORS ABOUT THIS, AND THEY SEEM TO RECOGNIZE THE PROBLEM, BUT THEY DON'T REALLY SEEM TO BE MOVING AT MORE THAN A SNAIL'S PACE.

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CHAIRMAN GOLDSTEIN: SO A SENSIBLE CONCLUSION FROM THIS PART OF THE CONVERSATION IS THAT NEURO SHOULD TRY TO LEAD THE WAY ON MAKING SURE THAT AWARDS ARE BIG ENOUGH AND LONG ENOUGH, AND THEN IT SHOULD PERCOLATE THROUGH THE REST OF CIRM'S AREAS.

DR. LEVITT: YEAH. I THINK THAT'S A REALLY GOOD SUMMARY. AND, AGAIN, IT CAN BE DONE THROUGH RFA'S WHERE IN CASE THERE ARE ISSUES ABOUT, WELL, WHY IS THAT GROUP GETTING IT OR WHATEVER? BUT WHEN YOU HAVE SPECIFIC RFA'S, YOU'RE FOCUSING, AND ALL INSTITUTIONS DO THIS, NON-PROFITS, HHMI DOES IT NOW WHEN THEY USED TO NOT DO IT, NIH, OF COURSE, HAS BEEN DOING IT FOR DECADES WHERE RFA'S ARE USED TO REALLY PULL ON EMPHASIS AREAS. AND THE DOLLAR AMOUNTS AND THE LENGTH OF TIME AND ALL THOSE THINGS ARE RFA SPECIFIC. SO THAT'S SOMETHING WE CAN THINK ABOUT.

CHAIRMAN GOLDSTEIN: GOOD POINTS. JUDY.

DR. GASSON: VERY QUICKLY. I AGREE WITH WHAT'S BEEN SAID. AND THE THIRD COMPONENT, IN ADDITION TO DOLLAR AMOUNTS AND LENGTH OF TIME, IS PERCENT EFFORT COMMITTED. AND THIS CAME UP IN THE SAME CONVERSATION THAT WE ARE REFERENCING AND HAS COME UP IN THE PAST AS WELL, TO NOT PRECLUDE PEOPLE

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FROM BRINGING FUNDS IN FROM OTHER SOURCES TO FULLY FUND THEIR RESEARCH OPERATION.

CHAIRMAN GOLDSTEIN: GREAT POINT. SO OTHER QUESTIONS ABOUT THE DATA AS PRESENTED OR COMMENTS PLEASE?

DR. CANET-AVILES: I HAVE AN ANSWER ACTUALLY TO AN EARLIER QUESTION, LARRY. DO YOU WANT ME TO ANSWER? I THINK IT WAS DR. FISCHER-COLBRIE. HE WAS ASKING ABOUT THE RESEARCH THAT WE CAN SEE HERE FROM THIS IDEA TO DISCOVERY CANDIDATE THAT WE HAVE NOT SEEN MOVING FORWARD TO TRAN AND CLIN. AND THE MAIN ANSWER HERE IS THAT MANY OF THEM ARE EITHER STILL ACTIVE AWARDS OR IN ONE CASE, LET ME SEE, YES, IT WAS MOSTLY THAT THEY WERE ACTIVE AWARDS STILL. SO WE ARE -- IN ONE CASE ACTUALLY SOMEBODY IS CURRENTLY APPLYING THROUGH A COMPANY. SO THAT COULD BE. AND OUR TEAM IS NOW DISCUSSING DETAILS WITH THEM. SO IT IS STILL ALIVE.

MR. FISCHER-COLBRIE: TERRIFIC.

CHAIRMAN GOLDSTEIN: MARV, YOU'RE UP.

DR. SOUTHARD: I WAS JUST WONDERING IF WE ARE DOING ANY CURRENT OUTREACH TO INSTITUTIONS IN THE NEUROPSYCH AREA TO SEE MORE WHAT IT MIGHT TAKE? BECAUSE IN THIS LAST DISCOVERY, IN THE 85 NEW THINGS I SAW, I DIDN'T SEE ANY THAT WERE SPECIFICALLY IN

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THE NEUROPSYCH AREAS THAT I COULD DISTINGUISH ANYWAY.

CHAIRMAN GOLDSTEIN: SO COULD WE GO BACK TO ONE OF THE SLIDES THAT SHOWED FUNDING BY DISEASE BURDEN BECAUSE THIS GETS US INTO WHAT I THINK IS ANOTHER IMPORTANT QUESTION FOR US TO BE DISCUSSING, WHICH IS IS IT IMPORTANT FOR US TO ALLOCATE BY DISEASE BURDEN OR BY DISEASE FREQUENCY OR BY SOME OTHER METRIC OF DISEASE IN THE POPULATION, OR SHOULD WE CONTINUE TO BE COMPLETELY OPPORTUNITY ORIENTED BY QUALITY FOLLOWING REVIEW?

AND, YES, MARV, YOUR OBSERVATION WAS CORRECT. THE BURDEN OF NEUROPSYCHIATRIC DISEASE IS PRETTY IMPRESSIVE, AND THE AMOUNT OF CIRM FUNDING THAT WE'VE PUT IN THERE IS UNFORTUNATELY ALSO IMPRESSIVE.

DR. LEVITT: LARRY, WE HEARD FROM THE EXPERTS. I MEAN YOU KNOW QUITE WELL THAT THERE'S A REASON WHY INDUSTRY HAS PULLED BACK QUITE A BIT, PARTICULARLY IN NEUROPSYCHIATRIC DISORDERS. IT'S TOUGH SLEDDING, IT REALLY IS. SO WE HAVE TO HAVE A DOSE OF REALITY, LIKE THE LIMITATION ON GRANTS, THE LIMITS ON GRANTS IS IN LARGE PART DUE TO THE TOPIC AREA ITSELF, RIGHT. IT LOOKS BETTER IF -- AUTISM SPECTRUM DISORDER IS A DSM-V DIAGNOSED DISORDER. SO

THAT COULD GO INTO NEUROPSYCH. SO THE NUMBERS LOOK A LITTLE BETTER, BUT IT'S JUST REALLY DIFFICULT. AND I THINK WE CAN DO OUTREACH AND ALL THAT, AND WE CAN IMPROVE THINGS CERTAINLY BECAUSE WE HEARD SOME GREAT PEOPLE WHO WERE IN CALIFORNIA, BUT IT'S REALLY GOING TO BE SLOW. IT'S NOT FOR LACK OF TRYING, BUT IN THESE AREAS IT'S JUST REALLY, REALLY DIFFICULT. THERE'S NOT ENOUGH -- AND I THINK SEVERAL OF THE INVESTIGATORS TALKED ABOUT THIS WHO PRESENTED TO US. THERE'S STILL A TON OF DISCOVERY TO DO IN THIS AREA OF PSYCHIATRIC DISORDERS AND BRAIN DYSFUNCTION, JUST IS.

CHAIRMAN GOLDSTEIN: GREAT POINTS. VITO.

DR. IMBASCIANI: HI, EVERYONE. ROSA, THANK YOU FOR THESE SLIDES. THEY'RE VERY POWERFUL SHOWING THE DISCREPANCY BETWEEN THE DOLLARS SPENT, THE GRANTING, AND THE DISEASE BURDEN. AND PICKING UP ON SOMETHING BOTH MARVIN AND MARK JUST ALLUDED TO, IF I CAN TEASE IT OUT AS A QUESTION. AND PAT WAS JUST SPEAKING TO IT. DO WE HAVE A FEELING, A QUANTIFICATION OF HOW MANY, GOING ALL THE WAY BACK TO 2007, HOW MANY APPLICATIONS HAVE BEEN MADE TO CIRM IN THESE AREAS, BUT PERHAPS WERE REJECTED? THAT WOULD TAKE SOMEBODY -- AND IF WE DON'T HAVE A QUANTITY, DO WE HAVE SOMEBODY WITH A LONGER

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INSTITUTIONAL MEMORY THAN MINE THAT JUST HAS AN ANECDOTAL FEELING LIKE WE'VE SEEN A FEW OF THESE BEFORE AND WE REJECTED THEM BECAUSE I'D LIKE TO KNOW WHY. MAYBE IT WAS JUST PREMATURE. THE SCIENCE HADN'T DEVELOPED.

I DON'T KNOW WHETHER THAT QUESTION GOES TO JENN OR TO GIL OR ABLA. I DON'T KNOW.

DR. CREASEY: I HAVE POTENTIALLY A SCIENCE EXPLANATION. WHEN IT COMES TO THE PROJECTS WITH SMALL MOLECULES AND LARGE MOLECULES, WE ALWAYS ASK FOR THE PROJECT TO BE INVOLVED WITH STEM CELLS OR PROGENITOR STEM CELLS. AND SO THAT REASON, WE HAVE NOT ALLOWED ANY SMALL MOLECULES OR LARGE MOLECULES THAT DON'T HAVE THAT ASSOCIATION. UNTIL RECENTLY GENE THERAPY HAS BECOME MORE POPULAR. BUT FOR THAT REASON, TRAN AND CLIN HAVE NOT HAD ANY PROJECTS THAT DEALT WITH NEUROPSYCH BECAUSE THE SMALL MOLECULES WOULD HAVE TO BE ACTING OR INVOLVING STEM CELLS. AND IT'S VERY HARD IN THE NEUROGENESIS AREA. THERE IS STILL KIND OF A LACK OF AGREEMENT WITH MANY OF THE SCIENTISTS AS TO WHETHER COMPOUNDS THAT AFFECT NEUROGENESIS ACTUALLY INVOLVE STEM CELL OR PROGENITOR.

SO THAT'S JUST ONE SCIENTIFIC EXPLANATION AS TO WHY WE DON'T HAVE ANY IN TRAN AND CLIN.

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CHAIRMAN IMBASCIANI: I WANT TO ASK --

DR. CANET-AVILES: FROM A -- I WAS GOING TO COMPLIMENT MY COLLEAGUE, DR. IMBASCIANI.

CHAIRMAN IMBASCIANI: NO. NO. I THINK YOU WANT TO FOLLOW UP ON THAT. I WAS GOING TO ASK A FOLLOW-UP QUESTION. GO AHEAD.

DR. CANET-AVILES: I WAS GOING TO COMPLIMENT THE EXCELLENT ANSWER FROM DR. CREASEY. IN TERMS OF DISCOVERY, WE HAVE NOT SEEN MANY. AND THE REASON IS A DIFFERENT REASON. IT COULD BE THE STUDY OF DISEASE MECHANISMS. THAT WAS NOT ONE OF OUR PRIORITIES, BUT ALSO AT THE TIME THE SCIENCE, THE MODELS WERE NOT AS READY AS WE HAVE NOW, WHICH IS SOME OF THE FOCUS THAT DR. GOLDSTEIN HAS HAD IN THE PREVIOUS TASK FORCES TO SHOW THE READINESS OF THE FIELD IN TERMS OF DISCOVERY FOUNDATIONAL RESEARCH.

SO THAT WAS THE REASON. AND WE SAW A FEW. AND, IN FACT, ONE OF THE PEOPLE THAT HAD A MODEL THAT HAD APPLIED WAS ONE OF THE PEOPLE, DR. BRENNAND, WHO USED TO BE AT DR. RUSTY GAGE'S LAB. SO THAT'S ONE OF THE SINGLE PEOPLE THAT WE HAD IN NEUROPSYCHIATRIC DISEASES APPLY.

CHAIRMAN GOLDSTEIN: I'LL POINT OUT VITO'S QUESTION IS TILL PRETTY VALID. DO WE KNOW THAT WE

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DIDN'T GET A LOT OF NEUROPSYCHIATRIC APPLICATIONS IN THE PAST AND THEN TURN THEM DOWN?

DR. CANET-AVILES: YES. I ASKED THE QUESTION. I HAVE THE TEAM AT THE READY AND I ASKED. AND NOW WE HAVE DR. KELLY SHEPARD WHO HAS HISTORICAL MEMORY WHO'S BEEN WITH US FOR 13 OR 14 YEARS, AND SHE CONFIRMED THAT WE HAVE NOT GOTTEN MANY APPLICATIONS OVER THE YEARS IN THE NEUROPSYCHIATRIC DISCOVERY FIELD. THANK YOU, KELLY.

CHAIRMAN IMBASCIANI: IF I CAN JUST CLOSE OUT MY SET OF QUESTIONS. I'M NOT GOING TO ASK THIS QUESTION, BUT OUR CONVERSATION IS BEGGING THE QUESTION. AS WE EXPANDED ONCE BEFORE THE STEM CELL DEFINITION OF CIRM'S BASIS TO INCLUDE GENETIC THERAPY, IS THERE ROOM FOR A CONVERSATION GOING FORWARD TO EXPAND IT OR ALTER IT YET AGAIN IF WE IDENTIFY SUCH A HUGE NEED? I'M NOT ASKING THE QUESTION, JUST PLANTING THE SEED.

CHAIRMAN GOLDSTEIN: THANK YOU, VITO. A NUMBER OF US HAVE BEEN HAVING CONVERSATIONS ABOUT EXACTLY THIS ISSUE. ALTHOUGH I WILL POINT OUT THAT IF YOU WERE TO DO DRUG DISCOVERY IN THE NEUROPSYCHIATRIC AREA, YOU COULD BE USING STEM CELL-DERIVED MODELS FOR YOUR OPTIMIZATION ALL THE WAY THROUGH UP UNTIL YOU'RE IN CLINICAL TRIALS.

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STEVE.

MR. JUELSGAARD: YES. SO LET ME JUST FOLLOW ON VITO'S THOUGHT PROCESS FOR A MOMENT. SO AS YOU KNOW, DR. IMBASCIANI, WE DID THIS ONCE BEFORE. AND WE EXPANDED THE AREA IN WHICH WE'RE INVOLVED TO INCLUDE GENE THERAPY. IT'S NOT PART OF THE STEM CELL AREA. BUT WE DID IT BECAUSE THERE'S WORDING IN PROP 71 AND NOW IN PROP 14 CALLED OTHER VITAL RESEARCH. AND IT'S A HOOK TO HANG THINGS ON THAT ARE NOT STEM CELL BASED. SO IT'S PROVIDING 5.5 BILLION IN BOND FUNDING TO ALLOW CIRM TO CONTINUE FUNDING STEM CELL AND OTHER VITAL RESEARCH TO DEVELOP TREATMENTS AND CURES, TA-DA.

AND WHEN YOU LOOK SPECIFICALLY AT THE ONE AND A HALF MILLION, THERE'S NO REFERENCE IN THE ONE AND A HALF THAT IS STEM CELL BASED OR GENE THERAPY BASED. IT'S JUST A POT OF MONEY AIMED AT A PARTICULAR THERAPEUTIC AREA OR A PARTICULAR ORGAN OF THE HUMAN BODY, THE CENTRAL NERVOUS SYSTEM AND THE BRAIN.

SO I DO THINK THAT THERE PROBABLY IS, ALTHOUGH I WOULD DEFER TO SCOTT TOCHER AND RAFAEL, OUR GENERAL COUNSEL, AS TO WHETHER WE COULD USE THIS LANGUAGE TO BASICALLY BROADEN THE NET THAT WOULD BRING IN SMALL MOLECULES AND LARGE MOLECULES TO BE

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PART OF DEALING WITH CNS DISORDERS IF WE WANTED TO. BUT I DO AGREE. I THINK THE REAL ISSUE IS WE ARE STILL WAY BACK AT THE DISCOVERY STAGE OF TRYING TO UNDERSTAND HOW THESE THINGS WORK. THIS IS IN NEUROPSYCHIATRY NOW.

BUT, ANYWAY, THERE IS POTENTIALLY A PATHWAY TO BROADEN THE NET A BIT IF WE WANT TO, AT LEAST THAT'S MY IMPRESSION.

MR. TOCHER: STEVE, FOR WHAT IT'S WORTH, THIS IS SCOTT BACK AT CIRM. I THINK YOUR READING IS CORRECT. THE VITAL RESEARCH OPPORTUNITY LANGUAGE IN BOTH PROPOSITIONS DOES ALLOW US TO EXPAND THE TECHNOLOGY BASIS FOR THESE AWARDS.

MR. JUELSGAARD: THANK YOU, SCOTT.

MR. SACASA: I AGREE, STEVE. RAFAEL SPEAKING.

MR. JUELSGAARD: THANK YOU.

CHAIRMAN GOLDSTEIN: WELL, SINCE WE ARE GETTING PROGRESSIVELY MORE COMMITTED TO THE DEVELOPMENT OF NEUROPSYCHIATRIC PROGRAMS TO TRY TO REMEDY THIS VOID THAT WE HAVE, THIS MAY BE A GOOD AREA TO TEST SOME OF THOSE IDEAS OUT IN AND SEE HOW THEY GO.

LET ME JUST ASK IS THERE ANYTHING ELSE IN THE NEURO AREA THAT HAS BEEN NEGLECTED TO THE EXTENT

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THAT NEUROPSYCHIATRIC DISORDERS HAS BEEN? IS THERE SOMETHING ELSE THAT WE ARE MISSING?

CHAIRMAN IMBASCIANI: IS NEUROMUSCULAR INCLUDED IN SOME OF THE OTHER CATEGORIES?

CHAIRMAN GOLDSTEIN: ALS AND MOTOR NEURON DISEASE IS THERE, VITO. SO THAT WOULD BE ONE MAJOR FORM OF MUSCLE DISORDERS, BUT THAT WOULD NOT INCLUDE, FOR EXAMPLE, DUCHENNE MUSCULAR DYSTROPHY. THAT WOULD COME UP IN A DIFFERENT SET OF PROGRAMS.

JUDY.

DR. GASSON: IN SPEAKING TO SOME OF MY COLLEAGUES IN PSYCHIATRY, BECAUSE I AM NOT A NEUROSCIENTIST, THEY DID ASK IF TEAMS WERE BEING PUT TOGETHER, FOR EXAMPLE, WOULD IT BE POSSIBLE TO INCLUDE EXPERTS ON SOCIAL DETERMINANTS OF DISEASE AND IN SPECIFIC IN MENTAL ILLNESS. AND SO I SAID I WOULD ASK THE QUESTION HERE. PROBABLY MARV WOULD KNOW MORE ABOUT IT THAN I DO.

CHAIRMAN GOLDSTEIN: I THINK ALWAYS THE INITIAL ANSWER IS CAN YOU GET IT PAST THE REVIEWERS. BUT THERE COULD BE CARVE-OUTS IN RFA'S FOR THAT KNOWLEDGE IF THAT SEEMED APPROPRIATE. IT'S SOMETHING I HADN'T CONSIDERED, JUDY, BUT IT'S A GREAT POINT.

DR. LEVITT: I THINK IT'S HARD TO IMAGINE

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DOING IT IN THE MODEL SYSTEMS THAT CIRM IS FUNDING. AND THE QUESTION IS WHETHER -- MOST OF THE DISCOVERY AREAS ARE USING ANIMAL MODELS. AND SO -- AND I WORK IN THIS AREA. I THINK IT'S A MAJOR STRETCH AND VERY COMPLICATED BECAUSE THE GENOME IS FINITE AND THE SOCIAL DETERMINANTS ARE NOT. SO IT TURNS OUT TO BE REALLY COMPLICATED.

I WAS GOING TO SAY, GIVEN THE BURDEN AND ALSO GIVEN THE PREVALENCE, I'M SURPRISED ABOUT -- AND GIVEN THE POSSIBILITY OF USING THERAPEUTIC APPROACHES THAT IS THE BREAD AND BUTTER FOR CIRM IN THE INITIAL FOCUS, I'M SOMEWHAT SURPRISED ABOUT THE NUMBER OF -- THE AMOUNT OF FUNDING FOR STROKE. I DON'T KNOW WHY THAT IS. I DON'T KNOW HOW THE DOLLARS ARE DISTRIBUTED IN TERMS OF THE VARIOUS PROGRAMS, BUT THIS ISN'T DISC. IT MAY BE BECAUSE THE MODEL SYSTEMS ARE ANIMAL MODELS, ET CETERA. BUT I THINK THERE'S SO MUCH DISCOVERY ON THE MOLECULAR BASIS OF SELF-SURVIVAL AND THERAPEUTICS IN THAT AREA, THAT THIS IS ANOTHER AREA, I THINK, WOULD BE RIPE FOR TRYING TO EMPHASIZE, PARTICULARLY WHEN YOU LOOK AT THE BURDEN. IT'S BASICALLY TIED FOR NO. 2. AND THE NUMBER OF GRANTS THAT ARE LISTED HERE, PRETTY LOW.

CHAIRMAN GOLDSTEIN: MARIANNE OR ROSA OR

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SOMEBODY, CAN WE SEE THE SLIDES FOR TRAN AND CLIN TO GET A SENSE OF WHETHER STROKE CONTINUES TO HAVE THAT LEVEL OF RELATIVE FUNDING?

MR. JUELSGAARD: IF YOU LOOK AT SLIDE 13, THE ONLY STROKE SHOWING UNDER INDICATION IS THE ONE WITH STEINBERG AT STANFORD. OTHERWISE IT DOESN'T SHOW UP AS A SEPARATE CATEGORY. I IMAGINE ALL THE FUNDING, BECAUSE IF YOU FOLLOW THAT LINE THROUGH, WE ARE ALREADY AT CLIN2, BUT PROBABLY ALL THE FUNDING THAT'S ATTRIBUTED TO STROKE HAS GONE TO DR. STEINBERG AT STANFORD. THAT WOULD BE MY INTUITION ANYWAY.

DR. CANET-AVILES: SO THE ONE THAT WE SEE HERE, LIKE USUALLY STROKE HAVE LARGER GRANTS. THAT'S WHY WE SEE MORE IN TRAN AND CLIN WHEN MARIANNE SHOWED IT. THEY ARE MUCH MORE IN LATER STAGE. AS YOU CAN SEE HERE, WE HAVE -- AND I WILL LET ABLA SPEAK, ABLA OPINE HERE -- BUT STROKE IN TRAN AND CLIN IS AT A MUCH HIGHER RATING IN TERMS OF SPENDING.

DR. LEVITT: WELL, THAT'S GOOD NEWS.

CHAIRMAN GOLDSTEIN: MARK.

MR. FISCHER-COLBRIE: THE QUESTION ABOUT WHAT ARE WE MISSING, I WANT TO ASK A COROLLARY QUESTION WHICH I THINK HAS TO DO WITH NOT THE

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DISEASE INDICATION, BUT RATHER THE UNDERLYING ROOT CAUSE BECAUSE WE'VE FOUND OUT SO MUCH MORE IN THE LAST EVEN FOUR OR FIVE YEARS AROUND THE BRAIN-GUT AXIS RELATED TO MICROBIOME, FOR EXAMPLE. IT'S OFF THE CHART.

AND THE QUESTION MIGHT BE IS THERE SUFFICIENT FUNDING GOING INTO THE STUDY OF THAT AREA?

THE OTHER COROLLARY AREA HAS TO DO, AND AGAIN, SOME OF THAT'S TIED TO THE BRAIN-GUT AXIS WITH THE MICROBIOME, BUT IT'S SOMETHING THAT'S COMPLETELY SEPARATE IS MUCH GREATER INVOLVEMENT THROUGH THE MEN SYSTEMS ACROSS A WIDE RANGE OF NEURAL DISEASES THAN WHAT HAS EVER BEEN ANTICIPATED. AND ALSO POINT TO THE RELATIVELY RECENT DISCOVERY OF THE LYMPHATIC SYSTEM IN THE BRAIN WHICH IS A SHOCKING THING TO FIND OUT JUST A FEW YEARS AGO THAT IT EVEN EXISTED.

SO I WANTED TO ASK A QUESTION ALONG THOSE LINES AS WELL AS THE DISEASE INDICATION LINE BECAUSE SOME OF THIS ALSO GETS BACK TO CONSORTIA AND OTHER KINDS OF CONVERSATIONS THAT I THINK WE NEED TO HAVE. I DON'T KNOW IF ANYBODY CAN COMMENT ON THOSE TWO AREAS OF ARE THEY OPPORTUNITIES FOR FOCUS OR NOT.

CHAIRMAN GOLDSTEIN: THERE'S BEEN QUITE A

LOT OF WORK ON MICROGLIAL ROLES IN DIFFERENT NEURODEGENERATIVE DISORDERS. AND THAT'S A PART OF THE BRAIN'S IMMUNE SYSTEM. IT'S NOT B AND T-CELL SYSTEMS, BUT IT'S A REALLY IMPORTANT DETERMINANT OF HOW THESE DISEASES GO. AND SOME REALLY INCREDIBLE MODELING STUDIES HAVE APPEARED IN THE PAST SIX MONTHS THAT USE ORGANOIDS AND MICROGLIA TO TRANSPLANT, FOR EXAMPLE, INTO MOUSE BRAINS AND TRACKING THEIR BEHAVIOR FOLLOWING THEIR IN VITRO.

DR. CANET-AVILES: AND, DR. GOLDSTEIN AND MR. FISCHER-COLBRIE, SO FOR THE, AGAIN, THE CONCEPT THAT WE ARE GOING TO BE BRINGING IN SEPTEMBER, WE ARE TAKING ALL OF THESE ASPECTS INTO ACCOUNT. SO NEURO, IMMUNE AXIS IS INVOLVED IN NEURODEGENERATION, NEUROPSYCHIATRIC, NEURODEVELOPMENTAL. SO WE COULD BE PRIORITIZING THE SCOPE OF SOME RESEARCH, THE FACT THAT IT WILL BE MULTIDISCIPLINARY TYPE OF APPROACH COULD BE ENTICING IMMUNOLOGISTS TO WORK WITH NEUROSCIENTISTS TO TRY TO QUIZ THESE KIND OF MECHANISMS AND SORT THEM OUT THROUGH THE NEW PROGRAM THAT WE WILL BE BRINGING UP. SO I HOPE THAT ANSWERS YOUR QUESTION, BUT WE ARE TAKING IT INTO ACCOUNT. BECAUSE ONE OF THE WAYS THAT WE ARE THINKING ABOUT IT -- GO AHEAD.

MR. FISCHER-COLBRIE: NO. NO. PLEASE

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CONTINUE.

DR. CANET-AVILES: ANOTHER WAY THAT WE HAVE THOUGHT ABOUT IT, THERE IS THE MICROBIOME, THE GUT MICROBIOME, THERE IS THE VASCULATURE, THERE IS THE NEURO IMMUNE SYSTEM. BUT ANOTHER WAY TO LOOK AT IT -- SO WE COULD HAVE LOOKED AT THINGS LIKE THAT IN TERMS OF SYSTEMS INVOLVED AND PRIORITIZED, BUT THEN WE WOULD BE TAKING ONE OVER ANOTHER. SO PERHAPS THE WAY TO DO IT IS SAY NEUROPSYCHIATRIC AND THEN SAY TAKE A SYSTEMS APPROACH AND FIGURE OUT HOW THESE SYSTEMS ARE INVOLVED. AND THEN WE CAN COLLABORATE ALSO WITH PEOPLE THAT ARE BRINGING CONSORTIA FROM NEURODEGENERATION THAT HAVE NEURO-IMMUNE COMPONENTS.

SO THOSE ARE THINGS THAT WE ARE DISCUSSING. WE ARE TALKING TO DIFFERENT POTENTIAL CONSORTIA TO COLLABORATE IN THE FUTURE, AND THAT WILL BE BROUGHT UP IN THE VERY EXCITING CONCEPT THAT WE WILL BE PRESENTING IN SEPTEMBER.

MR. FISCHER-COLBRIE: GREAT. AND JUST THANK YOU VERY MUCH FOR PROMOTING ME TO DOCTOR. THAT'S QUITE AN HONOR, BUT UNFORTUNATELY I HAVEN'T QUITE GOTTEN THERE YET. SO IT'S SOMETHING I CAN LOOK FORWARD TO IN THE FUTURE PERHAPS. SO THANK YOU.

CHAIRMAN GOLDSTEIN: YOU GET AN HONORARY

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DOCTORATE, MARK.

MR. FISCHER-COLBRIE: HONORARY. THANKS.

CHAIRMAN GOLDSTEIN: I WANT TO MAKE A COMMENT ABOUT THE SOCIAL DETERMINANTS OF DISEASE AND REMIND PEOPLE THAT IT'S NOT NECESSARILY THE CASE THAT THAT'S OFF LIMITS TO STEM CELL-BASED MODELING BECAUSE IT'S OFTEN THE CASE THAT DIFFERENT GENOMIC AND GENETIC VARIANTS MAKE PEOPLE SUSCEPTIBLE TO DIFFERENT SOCIAL STRUCTURES. A REALLY GOOD EXAMPLE IS OPIOID USE DISORDER WHERE IT'S VERY CLEAR THAT THERE'S A GENETIC COMPONENT TO PEOPLE WHO SUCCUMB TO OPIOID USE DISORDER AND THOSE WHO DO NOT.

DID I JUST DROP A SLEDGEHAMMER ON THE CONVERSATION? SORRY ABOUT THAT.

MR. FISCHER-COLBRIE: NO. WELL SAID.

CHAIRMAN GOLDSTEIN: WE MAY BE RUNNING DOWN HERE. ANY OTHER QUESTIONS ABOUT HOW WE ARE PRIORITIZING? I WILL POINT OUT TO PEOPLE ALSO TO REMEMBER THAT SOMETIMES A THERAPY THAT IS DEVELOPED FOR A VERY SEVERE RARE DISEASE, ONCE IT'S VALIDATED BY CLINICAL TRIALS AND SHOWN TO BE SAFE AND EFFECTIVE, CAN BE SPREAD INTO MUCH MORE COMMON DISEASE. SO WE DO WANT TO TAKE THE DISTRIBUTIONS WITH A BIT OF A GRAIN OF SALT. PARKINSON'S AND ALZHEIMER'S THERAPIES MAY WORK FOR EACH OTHER, ET

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CETERA. BUT I HAVE TO SAY PERSONALLY I STILL FIND THE NEUROPSYCH NUMBERS PRETTY COMPELLING.

SO LET'S THEN TURN THE CONVERSATION TO THE OTHER SORT OF ISSUE ABOUT PRIORITIZING IN THINKING ABOUT A SET-ASIDE OR A MINIMUM AMOUNT THAT SHOULD GO INTO THE NEURO AREA. TO WHAT DEGREE DO WE WANT TO LET THE CURRENT SYSTEM MORE OR LESS CONTINUE, WHICH IS GENERAL RFA'S AND THEN PRIORITY DECISIONS MADE ON THE BASIS OF REVIEW VERSUS HOW MUCH TOP-DOWN INTERVENTION DO WE WANT TO MAKE IN THE SPECIFICITY OF RFA'S; FOR EXAMPLE, AN RFA SPECIFIC FOR NEUROPSYCHIATRIC DISEASE OR ALZHEIMER'S DISEASE OR SOMETHING ELSE BECAUSE WE FELT THERE WAS THE NEED?

DR. LEVITT: MY OWN PERSONAL FEELING, LARRY, IS THAT RFA'S CAN WORK QUITE WELL. I THINK THE CIRM TEAM NEEDS TO THINK ABOUT WHETHER THEY WANT TO PROMOTE A TEAM SCIENCE APPROACH. SO THE CONTE CENTERS AT NIMH, WHEN YOU LOOK AT THE DOLLARS SPENT AND THE RETURN ON INVESTMENT, SO SOME OF THE NEWER THERAPEUTICS CAME OUT OF CONTE CENTERS. THESE ARE FOUR, FIVE PROJECTS WITHIN THE CONTEXT OF A CENTER, AND THE CENTERS CAN BE DISTRIBUTED GEOGRAPHICALLY. BUT THE ONES THAT WERE AT YALE AND ROCKEFELLER AND PITTSBURGH, THEY'VE MADE A LOT OF PROGRESS BECAUSE YOU JUST MAKE A LOT MORE PROGRESS ON VERY DIFFICULT

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PROBLEMS WHEN YOU USE THIS KIND OF APPROACH.

SO I WOULD REALLY FAVOR THEM LOOKING CLOSELY, AND YOU CAN DO AN EVALUATION OF HOW THOSE CONTE CENTERS -- IT WAS NAMED AFTER A HOUSE OF REPRESENTATIVE PERSON FROM CONNECTICUT, BUT THEY'RE ESSENTIALLY PROGRAM PROJECTS. AND THEY CAN BE CLINICALLY FOCUSED, THEY CAN BE -- A LOT OF THEM ARE TRANSLATIONAL FOCUSED AND THEY WOULD FIT INTO THE TRANS DOMAIN, BUT I THINK RFA'S LIKE THAT WOULD ATTRACT, AND WITH ENOUGH MONEY, THEY WOULD ATTRACT REALLY HIGH QUALITY PROJECTS. AND THERE'S NO BETTER PLACE THAN CALIFORNIA TO DO THAT BECAUSE OF THE RESEARCH TALENT THAT'S HERE.

CHAIRMAN GOLDSTEIN: YEAH. IT'S A GREAT POINT. WE REALLY OUGHT TO LOOK AT OTHER GRANTING AGENCIES AND ASK WHAT SORTS OF MECHANISMS HAVE THEY FOUND TO BE VERY SUCCESSFUL THAT WE MIGHT WANT TO IMPORT INTO OUR OWN PROCESSES.

STEVE.

MR. JUELSGAARD: SO TO SORT OF FOLLOW UP ON THAT, AND THIS IS VERY MUCH AN OFF-THE-WALL THOUGHT, BUT THE IDEA, ONE IDEA IS TO AWARD A SUBSTANTIAL AMOUNT OF MONEY. AND LET ME JUST FOR THE SAKE OF THIS DISCUSSION TO TRY AND MAKE IT A LITTLE MORE TANGIBLE IS TO SAY WE'RE WILLING TO

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PROVIDE A $20 MILLION GRANT TO WHETHER IT'S ONE ORGANIZATION OR SEVERAL ORGANIZATIONS THAT GET TOGETHER TO DO SOME RESEARCH -- AND THIS IS IN THE NEUROPSYCHIATRY AREA -- TO DO SOME RESEARCH THAT'S A LITTLE MORE DIRECTED. SO THEY WOULD COME UP WITH THE IDEA OF WHAT THE DIRECTED RESEARCH WOULD BE ABOUT, WHO THE PARTICIPANTS ARE GOING TO BE, AND WHAT THE OUTCOME IS, BUT WE'D BE WILLING TO PROVIDE, AND THIS IS SOMETHING WE DON'T DO NOW OBVIOUSLY, BUT A SIGNIFICANTLY LARGE AMOUNT OF MONEY THAT'S GOING TO TAKE MORE THAN THREE YEARS TO GET DONE LIKELY, BUT IT WILL MAKE A SIGNIFICANT ADVANCEMENT IN OUR UNDERSTANDING OF, FIRST OF ALL, THE GENETICS OF NEUROPSYCHIATRIC DISEASES AS WELL AS POTENTIAL POINTS OF INTERVENTION IN THE PATHWAYS THAT ARE INVOLVED.

SO, AGAIN, JUST MAYBE A HAREBRAINED IDEA, BUT I THINK, GIVEN WHERE WE ARE AT IN THIS SITUATION, IT MAY BE THAT WE JUST NEED TO REALLY UP THE ANTE HERE TO ATTRACT PEOPLE AND MOVE THE BALL FORWARD.

CHAIRMAN GOLDSTEIN: IT'S A GREAT POINT. AS SOMEBODY WHO RAN A LAB NOT TOO LONG AGO, COSTS CAN JUST KILL YOU. AND GRANT RATE INCREASES YEAR OVER YEAR JUST DON'T KEEP PACE WITH INFLATION.

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MARV.

DR. SOUTHARD: I JUST WANTED TO SAY I THOUGHT STEPHEN'S IDEA WAS GREAT. I THINK WE SHOULD CONSIDER SOMETHING LIKE THAT.

DR. CANET-AVILES: I CAN ANSWER THAT -- SO FOR NEUROPSYCHIATRIC DISCOVERY, WE ARE DEVELOPING -- THE CONCEPT THAT WE'VE DEVELOPED THAT WE ARE GOING TO BE BRINGING IS RESPONDING TO THIS IDEA. SO YOU WILL SEE IT STRUCTURED IN THAT WAY, AND I THINK IT'S SOMETHING TO BE VERY EXCITED FOR.

THE SECOND THING IS IN TERMS OF PROGRAM PROJECT GRANTS, WHICH ARE MULTIDISCIPLINARY, LONG-TERM, WE HAVE TAKEN THE EXPERIENCE THAT WE HAVE AS A TEAM, WE'VE ALL WORKED IN DIFFERENT, SO I PERSONALLY WORK WITH THE NIA AND THE NIMH AND NINDS IN THE DIFFERENT ACCELERATING MEDICINES PARTNERSHIP FOR SCHIZOPHRENIA, PARKINSON'S, AND ALZHEIMER'S, WHICH WERE CONSISTING OF PROGRAM PROJECT GRANTS. AND WE'VE TAKEN THAT EXPERIENCE AND WE'VE ACTUALLY IMPLEMENTED IT IN THE STRUCTURE THAT WE ARE GOING TO BRING IN SEPTEMBER. SO, AGAIN, I THINK WE HEAR THAT LOUD AND CLEAR FOR THIS PROGRAM IN NEUROPSYCH.

CHAIRMAN GOLDSTEIN: MARK.

MR. FISCHER-COLBRIE: I THINK THOSE ARE BOTH FANTASTIC COMMENTS FROM BOTH STEPHEN AND ROSA.

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AND I THINK THAT'S EXACTLY THE KIND OF APPROACHES THAT WE NEED TO HAVE TO HAVE A CONCENTRATED GAME PLAN AND TO HAVE MULTIDISCIPLINARY GROUPS INVOLVED BECAUSE IT'S GOING TO REQUIRE DIFFERENT WAYS OF DOING THINGS THAN JUST RANDOM PEOPLE SUBMITTING PROPOSALS AND FOR RANDOM STUDY ACTIVITIES. SO I CONCUR ON BOTH OF THOSE COMMENTS AND BOTH WELL SAID. SO THANK YOU.

CHAIRMAN GOLDSTEIN: GREAT POINT. OTHER THOUGHTS ABOUT THESE ISSUES OF SPECIFYING PRIORITIES VERSUS PASSIVE REVIEW -- WELL, SEMI-PASSIVE?

SO -- MARK, GO AHEAD.

MR. FISCHER-COLBRIE: YEAH. WE ADDRESSED THE FIRST QUESTION, RIGHT. IS THAT SOMETHING WE WANT TO TRY TO TAKE A STAB AT? OR HOW DO WE WANT TO FRAME THE CONVERSATION AROUND NO. 1 THERE?

CHAIRMAN GOLDSTEIN: WELL, LET ME JUST THROW OUT A POSSIBILITY. IT SEEMS TO ME THAT BY AND LARGE THE BROAD RFA REVIEW-BASED SYSTEM FOR SETTING PRIORITIES DOES A GENERALLY GOOD JOB. IT DOESN'T HIT EVERYTHING BY DISEASE BURDEN NECESSARILY, BUT THE FLAWS, IF ANY, IS THAT IT SOUNDS LIKE GRANT SIZES JUST HAVEN'T BEEN BIG ENOUGH AND GRANT TERMS NEED TO BE A LITTLE BIT LONGER TO COPE WITH SOME OF THE EXPERIMENTAL CHALLENGES IN SOME OF THESE AREAS.

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MY PERSONAL VIEW WOULD BE THAT WE SHOULD DO WHAT WE ARE DOING WITH NEUROPSYCHIATRIC, WHICH IS WE'VE IDENTIFIED AN AREA THAT IS OBVIOUSLY, WOEFULLY UNDERINVOLVED WITH OUR AGENCY AND NEEDS WORK AND CONTINUE TO BE ALERT TO THINGS THAT WE'RE NOT DOING THAT LOOK LIKE THEY SHOULD BE PROFITABLE, BUT THAT OTHERWISE I WOULD NOT BE IN FAVOR OF SUBSTANTIAL PROGRAMMING OF THE ENTIRE ONE AND A HALF BILLION, SAY. I THINK WE HAVE TO RELY ON THE COMMUNITY TO TELL US WHAT'S SCIENTIFICALLY EXCITING, VALID, AND FEASIBLE.

MR. FISCHER-COLBRIE: IS THAT SOMETHING, THOUGH, THAT MAYBE A THIRD MIGHT BE A CONSIDERATION FOR SOMETHING LIKE THAT THAT'S A LITTLE BIT MORE DIRECTED TO BE ABLE TO PULL PEOPLE TOGETHER, OR IS THERE SOME OTHER NUMBER THAT MIGHT MAKE SENSE?

CHAIRMAN GOLDSTEIN: GREAT QUESTION. SOMEBODY ELSE WANT TO TAKE A STAB AT THIS?

DR. LEVITT: I PERSONALLY FEEL, LARRY, IT'S HARD TO THINK OF A -- WHAT SIZE OF THE PIE, WHAT PIECE WITHOUT SEEING THE RFA'S. I AGREE WITH YOU, THAT IT SHOULD NOT BE THE WHOLE NUT, RIGHT. IT CAN'T BE FOR ALL THE REASONS THAT YOU'VE SAID. SO I DON'T KNOW WHERE TO TITRATE THIS, BUT I THINK THE IDEA THAT WE'VE HEARD ABOUT REALLY PUTTING AN

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EMPHASIS ON PUSHING TEAMS AND FUNDING AT A HIGHER LEVEL BECAUSE OF WHAT WE ARE FACED WITH, NOT CIRM, BUT FAMILIES AND INDIVIDUALS WHO ARE SUFFERING IS THE RATIONALE FOR REALLY RAMPING THIS UP. BUT I DON'T KNOW WHAT THE NUMBER IS. IT SHOULDN'T BE ALL OF IT FROM MY PERSPECTIVE BECAUSE I AGREE WITH YOU, THAT YOU'VE GOT TO HAVE SOME GRASS-ROOTS DEVELOPMENT. YOU NEVER KNOW WHERE A GREAT IDEA IS GOING TO COME FROM. SO WE DON'T WANT TO BE PRESCRIPTIVE FOR ALL OR EVEN A MAJORITY OF IT. I DO THINK IT COULD BE A REASONABLE SIZE OF THIS, AND IT WOULD MAKE A HUGE DIFFERENCE.

MR. TOCHER: LARRY, WE HAVE A COUPLE COMMENTS HERE FROM THE CIRM TEAM IF THAT'S OKAY.

CHAIRMAN GOLDSTEIN: OH, YES, PLEASE. OF COURSE.

DR. MILLAN: THANK YOU SO MUCH. SO THE TEAM HAS BEEN LOOKING AT KIND OF WHAT OUR HISTORIC SPEND HAS BEEN IN TERMS OF PERCENTAGE OF THE DISCOVERY PROGRAMS KIND OF COMING IN THROUGH THE PILLAR PROGRAM. AND BASED ON THE ESTIMATE OF WHAT ROSA AND THE TEAM ARE WORKING ON FOR WHAT A CONCEPT FOR THIS COLLABORATIVE RESEARCH MODEL, LIKE A PROGRAM PROJECT GRANT-LIKE MODEL AND HER ESTIMATE FOR WHAT THAT WOULD COST ALL IN VERSUS WHAT THE

TARGET IS FOR TRANSLATIONAL, CLINICAL STAGE PROGRAMS, WE THINK THAT IT IS VERY FEASIBLE TO STILL CONTINUE THE PILLAR PROGRAMS, MEANING THE ONES THAT COME IN ORGANICALLY AND BE ABLE TO HAVE ENOUGH TO ACCOMMODATE A GOOD AMOUNT OF THOSE PLUS PROBABLY FUND, IF THE BOARD APPROVES TO THE SCALE THAT ROSA MAY PROPOSE, PROBABLY FOUR BIG PROGRAM PROJECTS. WE'LL STILL BE ABLE TO SUPPORT BETWEEN SEVEN AND TEN TRANSLATIONAL, CLINICAL STAGE PROGRAMS A YEAR.

JUST AS A BACK OF THE ENVELOPE, THAT WOULD STILL BE ACCOMMODATED BY THE MINIMUM OF THE $1.5 BILLION IN SPENDING. OF COURSE, MORE OF THE RESEARCH BUDGET COULD BE UTILIZED IF THERE WAS SOME PROMISING DIRECTION, THE BOARD COULD DECIDE THAT MORE OF THE RESEARCH ALLOCATION CAN BE PUT TOWARD THE CNS PROGRAMS. BUT I THINK THAT EVERYTHING THAT THE BOARD MEMBERS ARE PROPOSING TODAY COULD BE ACCOMMODATED. IT'S A COMBINATION OF UTILIZING THE STANDARD PILLAR PROGRAMS PLUS A MORE DIRECTED SIGNIFICANT INVESTMENT IN THESE PROGRAM PROJECT-LIKE GRANTS WHILE NOT COMPROMISING THE TRANSLATIONAL, CLINICAL PORTFOLIO.

CHAIRMAN GOLDSTEIN: THOSE ARE GREAT POINTS, MARIA. AND WE COULD LOOK AT IT AS WE ARE TAKING NEUROPSYCHIATRIC AS AN EXAMPLE AND WE ARE

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BUILDING IT UP, AND WE CAN SEE WHAT THE RATE LOOKS LIKE AT WHICH SPENDING IS GOING TO NEED TO INCREASE TO KEEP IN STEP WITH DEMAND AND BURDEN.

DR. MILLAN: RIGHT. SO THIS IS JUST CHARTING IT OUT BASED ON FORECASTING, LET'S SAY, IN THE INSTANCE OF SUCCESS AND YOU'RE ABLE TO FUND FOUR OF THESE BIG PROGRAMS, YOU'LL STILL BE ABLE TO ACCOMMODATE THE ORGANIC INFLOW OF NEW DISCOVERY RESEARCH AT PRETTY MUCH THE SAME RATE, ACCOUNTING FOR RECURRING ALLOCATIONS, AND STILL TRANSLATIONAL AND CLINICAL PROGRAMS.

BUT ABLA CREASEY, WHO HEADS OUR THERAPEUTICS DEVELOPMENT PROGRAM, WANTED TO ADD SOMETHING TO THAT AS WELL.

DR. CREASEY: I JUST WANTED TO GO BACK TO WHAT MR. JUELSGAARD MENTIONED, THE VITAL RESEARCH OPPORTUNITY. WOULD THE COMMITTEE CONSIDER, WITH YOUR LEADERSHIP, DR. GOLDSTEIN, THINKING OF SMALL MOLECULES AND POTENTIALLY LARGE MOLECULES AS POTENTIAL NEW OPPORTUNITIES TO FUND FOR TRAN AND CLIN AS A VITAL RESEARCH OPPORTUNITY TO COMPLEMENT WHAT IS GOING TO HAPPEN WITH DISCOVERY?

CHAIRMAN GOLDSTEIN: I THINK IT'S CERTAINLY SOMETHING WE SHOULD LOOK AT, ALTHOUGH I DO THINK THAT THE USE OF STEM CELL MODELS TO BE

OPTIMIZING GRANTS AND OPTIMIZING PROGRESS AND TO IDENTIFY SUBPOPULATIONS THAT ARE LIKELY TO RESPOND TO A GIVEN SMALL MOLECULE IS A WAY TO KEEP IT IN THE RANCH AT LEAST A LITTLE BIT. SO...

DR. CREASEY: AS POINTED OUT WITH THE DISCUSSION WE HAD IN THE SECOND NEURO TASK FORCE MEETING, IT'S GOING TO TAKE SEVERAL YEARS BEFORE SUCH MOLECULES OR SUCH COMPOUNDS ARE LIKELY TO SCORE AND MOVE TO TRAN. AND AS YOU KNOW, TRAN TAKES TWO, THREE YEARS AND CLIN TAKES FOUR YEARS. WE CAN HAVE BOTH OPTIONS. IT'S YOUR CHOICE OBVIOUSLY.

CHAIRMAN GOLDSTEIN: IT'S CERTAINLY AN IMPORTANT DISCUSSION FOR US TO CONTINUE.

I THINK THE OTHER QUESTION IS GOING TO BE THE USE OF PRIMARILY NOVEL CHEMICAL ENTITIES, NCE'S, WHICH IS, OF COURSE, THE WAY IT'S DONE IN INDUSTRY BECAUSE THEY'RE PATENTABLE VERSUS CONTINUING TO MINE THROUGH EXISTING DRUG-LIKE MOLECULES, FDA-APPROVED DRUGS, DRUGS THAT HAVE BEEN PROVEN TO BE SAFE BUT DIDN'T WORK WELL FOR THE CHOSEN INDICATION, ET CETERA, ET CETERA.

DAVID HIGGINS.

DR. HIGGINS: YES. THIS IS PROBABLY OBVIOUS, BUT DO WE HAVE ANY WAY OF KNOWING OR CAN WE HAVE A WAY TO KNOW WHY GRANTS THAT ARE INITIALLY

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APPROVED FAIL, THEY EITHER DON'T COME BACK PRESUMABLY BECAUSE THEY HAVE SOME INSIGHT AS TO THEIR PROGRESS, OR THEY RESUBMIT IN THE NEXT STAGE AND THEY'RE JUST NOT HIGH ENOUGH LEVEL TO BE APPROVED? I MEAN IT SEEMS LIKE WE'RE WILLING -- EVERYTHING IS ON THE TABLE. I'M HEARING ALL THESE POSITIVE RECEPTION ON THE STAFF'S PART TO CHANGING THE WAY WE DO THINGS. CAN WE CHANGE THE WAY WE DO THINGS AND INCLUDE WHY HAVE PEOPLE FAILED IN THE PAST?

CHAIRMAN GOLDSTEIN: BOY, IS THAT A GOOD QUESTION. AND PERSONALLY SPEAKING, THERE'S A LOT OF DIFFERENT WAYS TO FAIL.

DR. LEVITT: GREAT POINT, LARRY.

CHAIRMAN GOLDSTEIN: I DON'T KNOW. HAS THE CIRM TEAM DONE ANY ANALYSIS OF THIS RETROSPECTIVELY? I'LL MAKE THE QUESTION.

DR. MILLAN: LARRY, CAN YOU HEAR ME?

CHAIRMAN GOLDSTEIN: GO AHEAD, MARIA.

DR. MILLAN: SO THE TEAM HAS BEEN -- WE CERTAINLY HAVE, BASED ON WHAT YOU HEARD FROM ROSA'S REPORT, NOT ENOUGH IN TERMS OF PROJECTS IN THE PIPELINE, AND SOME OF THEM ARE STILL ONGOING. BUT AS YOU KNOW, FOR TRADITIONAL DRUG DISCOVERY, WHEN YOU HAVE, EVEN FOR A SMALL MOLECULE, YOU START OFF

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WITH 10,000 COMPOUNDS AND AT THE END YOU'LL HAVE ONE PRODUCT. SO IT'S JUST PART OF IT IS THE NATURE OF WHAT THE PATH IS FROM DISCOVERY ALL THE WAY TO TRANSLATION AND CLINICAL. I THINK KIND OF THE VALUE PROPOSITION OR THE PROSPECT THAT WE HAVE THAT'S VERY EXCITING IS THAT WHEN WE HAVE A THERAPEUTIC THAT DEVELOP IN THE CELL AND GENE THERAPY PORTFOLIO, IT'S A DEFINITIVE TREATMENT. SO THAT IS -- THE IMPACT FACTOR AND THE VALUE OF THAT IS WONDERFUL ONCE YOU HAVE THAT.

SO I DON'T THINK IT'S UNUSUAL TO HAVE MANY PROGRAMS IN THE EARLY STAGES WHERE IT REALLY IS JUST LOOKING AT THE SCIENCE. IN SCIENTIFIC RESEARCH, NOT EVERYTHING WORKS OUT. IT MAY LEAD DOWN A DIFFERENT PATH. SAME THING WITH M-RNA, HOW M-RNA WAS FIRST LOOKED AT FOR A VARIETY OF INDICATIONS, INCLUDING BEING ABLE TO HAVE A BETTER WAY TO REPROGRAM IPSC, AND THEN NOW IT'S UTILIZED FOR VACCINES AND NOW WE SAW AN EARLY OUTCOME FROM AN EARLY PARKINSON'S -- I MEAN PANCREATIC CANCER TRIAL WITH M-RNA.

SO I THINK IT'S A MATTER OF JUST IT'S REALLY DIFFICULT TO VIEW IT PROJECT BY PROJECT. I THINK IF YOU'RE ABLE TO TAG THESE THINGS AND THEN FOLLOW THEM THROUGH ITS COURSE, ONE MAY SEE THAT IT WOULD LEAD TO A DIFFERENT TYPE OF THERAPEUTIC. SO

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IT'S NOT SOMETHING THAT IT'S REALLY EASY TO ANALYZE, BUT I THINK THAT'S THE REASON WHY BASIC AND FOUNDATIONAL AND MECHANISTIC RESEARCH IS VERY IMPORTANT BECAUSE YOU DON'T HAVE AN ANSWER YET. AND IT GIVES RISE TO POTENTIAL KNOWLEDGE TO LEAD TO ANSWERS.

BUT WHERE WE CAN TRACK A LITTLE BIT BETTER IS WHEN IT'S IN THE KIND OF THE LATER STAGES, TRANSLATIONAL TO PRECLINICAL TO CLINICAL. THERE WE HAVE A BETTER ACCOUNTING FOR WHY THINGS FAIL. SO WE HAVE A REALLY GOOD SENSE OF KIND OF SOME OF THE HURDLES. AND THOSE WE ARE TRYING TO ADDRESS THROUGH SOME OF OUR PROGRAMS AND HOW THE TEAMS ARE MANAGING THEM THROUGH MANUFACTURING INITIATIVES, THROUGH REGULATORY TYPE APPROACHES. AND SO THOSE ARE THE TYPES OF THINGS THAT ABLA HAS PRESENTED IN KIND OF HER PRESENTATION. IT'S STILL NOT 100 PERCENT OBVIOUSLY THAT WE CAN SOLVE ALL THE PROBLEMS FROM TRANSLATIONAL TO CLINICAL, BUT WE HAVE A BETTER IDEA IN THE LATER STAGES.

DR. CREASEY: BUT WE HAVE NOT HAD NEUROPSYCH THERAPIES IN OUR TRAN AND CLIN PROGRAMS, JUST TO BE CLEAR. WE HAVE NOT HAD ANY APPLY THAT FAILED OR SUCCEEDED.

DR. MILLAN: FROM ZERO PERCENT, WE HAVE A

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HUNDRED PERCENT SUCCESS RATE OF THEM NOT PROGRESSING.

DR. CREASEY: NOT PROGRESSING BECAUSE THEY HAVEN'T APPLIED.

DR. MILLAN: I THINK AS A GENERAL QUESTION, DR. HIGGINS, TO YOUR GENERAL QUESTION, IT'S JUST THE NATURE OF KIND OF DISCOVERY RESEARCH TO TRANSLATION TO CLINICAL. WE DO NOT EXPECT THAT THE PROGRESSION SHOULD BE VERY HIGH FROM THE DISCOVERY INTO TRANSLATIONAL. SOME OF IT IS ACTUALLY NOT INTENDED TO RISE TO THE PRODUCT PER SE. IT MAY START YOU ALONG A PATH WHERE IT LEADS TO DOWNSTREAM THERAPEUTIC CANDIDATE EVEN IF NOT DIRECTLY.

CHAIRMAN GOLDSTEIN: YEAH. WHEN YOU TALK TO PEOPLE IN THE TRENCHES, THEY'LL TELL YOU. IT'S HARDER THAN IT LOOKS.

OTHER COMMENTS OR QUESTIONS OR SHOULD I SUMMARIZE AND WRAP US UP?

DR. LEVITT: WHAT'S THE TIMELINE FOR THE TEAM PRESENTING? ROSA, YOU MENTIONED MULTIPLE TIMES WE'RE GOING TO SEE A VARIETY OF DIFFERENT PROPOSALS. I DON'T HAVE MY SCHEDULE IN FRONT OF ME. SO WHAT'S THE TIMELINE?

DR. CREASEY: SEPTEMBER.

DR. CANET-AVILES: DR. LEVITT, I THINK MARIANNE AND SCOTT HAVE THAT. SO I BELIEVE THE FIRST PRESENTATION TO THE SCIENCE COMMITTEE/TASK FORCE IS EITHER -- IS IN EARLY SEPTEMBER -- LATE AUGUST. IS THAT CORRECT, MARIANNE, LATE AUGUST? I KNOW YOU'RE SCHEDULING IT STILL.

MS. DEQUINA-VILLABLANCA: YEAH. I THINK THAT'S THE GENERAL TIMELINE, BUT THERE HASN'T BEEN ANYTHING CONFIRMED YET.

DR. LEVITT: OKAY. SO YOU'RE LOOKING AT THE LAST WEEK OF AUGUST, RIGHT?

DR. CANET-AVILES: THE LAST TWO WEEKS OF AUGUST AND THE FIRST TWO WEEKS OF SEPTEMBER, THE FIRST WEEK OF SEPTEMBER, I BELIEVE. THAT'S WHAT MARIANNE AND SCOTT WERE LOOKING INTO.

DR. LEVITT: ALL RIGHT. THANK YOU.

DR. CANET-AVILES: THAT COULD BE THE CONCEPT TO THE TASK FORCE/SCIENCE COMMITTEE BEFORE WE COME TO THE BOARD AT THE END OF SEPTEMBER, JUST TO CLARIFY.

DR. LEVITT: YEAH. THAT MAKES SENSE.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU.

DR. CANET-AVILES: EXCITING.

DR. LEVITT: YES, IT IS VERY EXCITING. AND IT SOUNDS LIKE YOU'VE DONE AN ENORMOUS HEAVY

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LIFT. THIS IS REALLY A TOUGH AREA. SO EVEN BEFORE I SEE IT, I'LL SEND MY CONGRATULATIONS TO THE TEAM. THIS IS REALLY --

DR. CANET-AVILES: THE TEAM. IT TAKES A BIG VILLAGE. AND THANKS TO ALL OUR COLLEAGUES. THANK YOU.

CHAIRMAN GOLDSTEIN: YOU GUYS HAVE BEEN DOING A GREAT JOB.

SO IF I WERE TO PROVIDE TENTATIVE ANSWERS TO THESE QUESTIONS FROM THE TASK FORCE, WHAT PERCENTAGE OF ONE AND A HALF BILLION DO WE WANT TO MAKE SPECIFIC RECOMMENDATIONS FOR, SOUNDS LIKE THE ANSWER IS NOT NECESSARILY A LARGE FRACTION. AND THAT THE THING TO DO, AT LEAST TO START, IS TO GET INTO AN AREA THAT WE HAVEN'T DONE BEFORE, MAKE SURE THE AWARDS ARE SUBSTANTIAL, AND SEE WHERE IT TAKES US.

AND AS TO OTHER IMPORTANT AREAS OF NEURO RESEARCH THAT WE ARE MISSING OTHER THAN NEUROPSYCHIATRIC, PAT MADE A GOOD COMMENT ABOUT STROKE. IT'S SOMETHING WE OUGHT TO HAVE ANOTHER LOOK AT, AT SOME POINT. WE CAN HAVE EXPERTS COME IN AND TALK TO US ABOUT WHAT'S GOING ON IN STROKE. I THINK THAT'S SOMETHING THAT WE COULD DO. BUT CERTAINLY LOOKING AT THE NEURODEGENERATIVES, IT

SEEMS LIKE WE HAVE PRETTY SUBSTANTIAL INVESTMENTS AND THAT THE AMOUNT OF THEM IS REASONABLY RELATED TO WHAT I, AT LEAST, KNOW OF OPPORTUNITY.

DO WE HAVE PUBLIC COMMENT AS PART OF THIS?

MR. TOCHER: MARIANNE.

MS. DEQUINA-VILLABLANCA: THERE CURRENTLY AREN'T ANY RIGHT NOW, LARRY.

CHAIRMAN GOLDSTEIN: GOOD. SO UNLESS THERE'S AN OBJECTION, I'M GOING TO MOVE THAT WE ADJOURN. I'M GOING TO POINT OUT THAT WE SHOULD LET OTHER MEMBERS OF THE TASK FORCE KNOW THAT THIS RECORDING WILL BE UP ON YOUTUBE. THEY SHOULD LOOK AT IT AND LET US KNOW WHAT THEIR IDEAS ARE.

SO OTHERWISE, THANK YOU ALL FOR YOUR TIME TODAY. VALUABLE CONVERSATION. AND WE WILL SEE YOU NEXT MONTH.

(THE MEETING WAS THEN CONCLUDED.)

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REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE VIRTUAL PROCEEDINGS BEFORE THE 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 JUNE 20, 2023, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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