

**BETH C. DRAIN, CA CSR NO. 7152**

BEFORE THE  
SCIENCE COMMITTEE OF THE  
INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE  
TO THE  
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE  
ORGANIZED PURSUANT TO THE  
CALIFORNIA STEM CELL RESEARCH AND CURES ACT  
REGULAR MEETING

LOCATION: VIA ZOOM

DATE: JANUARY 14, 2026  
12:30 P.M.

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

FILE NO.: 2026-2

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**I N D E X**

<b>ITEM DESCRIPTION</b>	<b>PAGE NO.</b>
<b>OPEN SESSION</b>	
1. CALL TO ORDER	3
2. ROLL CALL	3
3. CONSIDERATION OF THE RARE-DISEASE ACCELERATION THROUGH PLATFORM INNOVATION AND DELIVERY (RAPID) CONCEPT PLAN	4
4. DISCUSSION OF CIRM'S PORTFOLIO AND THE FUNCTION OF PREFERENCES	36
5. PUBLIC COMMENT	NONE
6. ADJOURNMENT	80

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JANUARY 14, 2026; 12:30 P.M.

CHAIRMAN FISCHER-COLBRIE: GREAT. LET'S  
CALL TO ORDER THE SCIENCE SUBCOMMITTEE AND WOULD  
LIKE TO HAVE SCOTT CALL THE ROLL.

MR. TOCHER: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MR. TOCHER: DEBORAH DEAS. MARK  
FISCHER-COLBRIE.

CHAIRMAN FISCHER-COLBRIE: HERE.

MR. TOCHER: ELENA FLOWERS.

DR. FLOWERS: PRESENT.

MR. TOCHER: JUDY GASSON. STEVE SMALE FOR  
JUDY GASSON.

DR. SMALE: HERE.

MR. TOCHER: VITO IMBASCIANI.

CHAIRMAN IMBASCIANI: HERE.

MR. TOCHER: PAT LEVITT.

DR. LEVITT: HERE.

MR. TOCHER: SHLOMO MELMED.

DR. MELMED: HERE.

MR. TOCHER: CAROLYN MELTZER.

DR. MELTZER: PRESENT.

MR. TOCHER: CHRIS MIASKOWSKI.

DR. MIASKOWSKI: PRESENT.

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1 MR. TOCHER: SHAUNA STARK.

2 DR. STARK: PRESENT.

3 MR. TOCHER: KAROL WATSON.

4 DR. WATSON: HERE.

5 MR. TOCHER: KEITH YAMAMOTO.

6 DR. YAMAMOTO: HERE.

7 MR. TOCHER: GREAT. THANK YOU VERY MUCH,  
8 KEITH. GREAT. WE HAVE A QUORUM. MARK.

9 CHAIRMAN FISCHER-COLBRIE: GREAT. THANK  
10 YOU SO MUCH. AND FIRST ORDER OF BUSINESS IS  
11 DR. SHYAM PATEL WILL PRESENT INFORMATION AND A  
12 PROPOSAL WITH RESPECT TO THE RAPID PROGRAM. SO,  
13 SHYAM, IF YOU'D LIKE TO TAKE OVER THE MEETING AND  
14 RESPOND TO QUESTIONS AS THEY COME UP, THAT WOULD BE  
15 GREAT.

16 DR. PATEL: GREAT. THANK YOU, MARK. I'M  
17 GOING TO SHARE MY SCREEN. HOPEFULLY EVERYONE CAN  
18 HEAR ME AND CAN SEE THE PRESENTATION. SO THANK YOU  
19 TO THE SCIENCE SUBCOMMITTEE CO-CHAIRS AND THE  
20 SCIENCE SUBCOMMITTEE FOR THE OPPORTUNITY TO PRESENT  
21 TO YOU TODAY.

22 I'M GOING TO BE PRESENTING THE RAPID  
23 FUNDING OPPORTUNITY ON BEHALF OF MY TEAMMATES,  
24 DR. JIM CAPANELLI AND DR. LISA MCGINLEY. AND THE  
25 RAPID FUNDING PROGRAM STANDS FOR RARE DISEASE

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1 ACCELERATION THROUGH PLATFORM INNOVATION AND  
2 DELIVERY.

3 SO I'LL START OFF WITH THE IMPACT GOAL AND  
4 THEN A SIGNIFICANT AMOUNT OF BACKGROUND ON WHY THIS  
5 INITIATIVE IS NECESSARY AND WHAT THE LANDSCAPE IS  
6 ENTERING INTO. AND THEN I'LL FOLLOW THAT UP WITH  
7 TALKING ABOUT THE ACTUAL FUNDING PROGRAM AND THE  
8 MECHANICS AND STRUCTURE OF THE AWARDS.

9 SO THE RAPID FUNDING OPPORTUNITY IS  
10 RESPONSIVE TO THE SAF GOAL 3, WHICH WAS TO ADVANCE  
11 FOUR TO SEVEN RARE DISEASE PROJECTS TO BLA. AND IN  
12 THAT IS ADDRESSING THE SITING RECOMMENDATION THAT  
13 WAS MADE TO THE BOARD, WHICH IS TO PILOT  
14 PLATFORM-BASED THERAPY DEVELOPMENT FOR GENE THERAPY.  
15 AND THIS IS TO CREATE A NEW MODEL FOR HOW TO  
16 ACCELERATE GENE THERAPY DEVELOPMENT FOR RARE  
17 DISEASES.

18 SO AS MANY OF YOU KNOW, THERE ARE AT LEAST  
19 10,000 UNIQUE RARE DISEASES IN THE PATIENT  
20 POPULATION TODAY. COLLECTIVELY THEY AFFECT OVER 30  
21 MILLION PEOPLE IN THE U.S. SO EACH RARE DISEASE MAY  
22 HAVE A SMALL POPULATION, BUT CUMULATIVELY THEY  
23 AFFECT OVER 30 MILLION PEOPLE. 50 PERCENT OF THESE  
24 RARE DISEASES ARE CHILDHOOD DISEASES AND 80 PERCENT  
25 HAVE A GENETIC BASIS.

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1           AND DESPITE THE VAST MAJORITY OF CELL AND  
2           GENE THERAPIES THAT HAVE BEEN APPROVED TO DATE HAVE  
3           BEEN TARGETING RARE DISEASES, 95 PERCENT OF RARE  
4           DISEASES HAVE NO APPROVED THERAPY. AND THIS IS DUE  
5           TO THE FACT THAT THE TRADITIONAL DRUG DEVELOPMENT  
6           PATHWAY IS SLOW, EXPENSIVE, AND DOESN'T REALLY ALLOW  
7           FOR MASS DEVELOPMENT AND PRODUCTION OF GENETIC  
8           THERAPIES FOR THE LARGE NUMBER OF RARE DISEASES THAT  
9           ARE AFFECTING THE POPULATION.

10           SO THIS SLIDE DESCRIBES BRIEFLY WHAT THE  
11           THERAPEUTIC DEVELOPMENT PATHWAY LOOKS LIKE. YOU'VE  
12           SEEN THIS IN VARIOUS DIFFERENT FLAVORS. ALTHOUGH  
13           GENETIC THERAPIES ENJOY A RELATIVELY FASTER TIMELINE  
14           THAN TRADITIONAL SMALL MOLECULES AND BIOLOGICS, IT  
15           STILL TAKES 10 TO 20 YEARS TO GO FROM THE FULL  
16           DEVELOPMENT LIFE CYCLE OF CANDIDATE DISCOVERY  
17           THROUGH APPROVAL FOR THESE THERAPIES. AND BECAUSE  
18           THE DEVELOPMENT OF EVERY SINGLE GENE THERAPY IS SO  
19           TIME, COST, AND RESOURCE INTENSIVE, IT REALLY IS  
20           VERY DIFFICULT TO DEVELOP GENETIC THERAPIES IN A  
21           MULTIPLEX MANNER. YOU'RE BASICALLY DEVELOPING EACH  
22           THERAPY ONE AT A TIME. AND WE OFTEN SEE THESE TYPES  
23           OF PROGRESSION PLOTS FOR COMPANIES AND ACADEMICS  
24           WHERE THEY SHOW ONE THERAPY BEING DEVELOPED AT A  
25           TIME IN A STAGGERED WAY.

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1 SO THERE HAS TO BE A BETTER WAY. WHAT IF  
2 THE DEVELOPMENT TIMELINE IS ACCELERATED? WHAT IF WE  
3 DEVELOPED DRUGS FASTER? SO THIS WAS RECENTLY  
4 EXEMPLIFIED BY THE CHILDREN'S HOSPITAL OF  
5 PHILADELPHIA'S EXPERIMENT WITH BABY KJ'S GENE  
6 EDITING THERAPY WHERE THEY WERE ABLE TO DEVELOP AND  
7 ADMINISTER WITHIN SIX MONTHS OF DIAGNOSIS THE  
8 GENETIC THERAPY FOR BABY KJ'S UREA CYCLE DISORDER.

9 HOWEVER, IN DEVELOPING THIS THERAPY, THEY  
10 HAD TO LARGELY DO ALL OF THE TESTING THAT YOU WOULD  
11 DO FOR A GENE THERAPY. SO THIS INCLUDED MULTIPLE  
12 ANIMAL MODELS, INCLUDING MOUSE AND NHP MODELS, AND  
13 ALL OF THE MANUFACTURING ASSOCIATED WITH THAT. SO  
14 WHILE THE TIMELINE WAS CONDENSED, IT WAS STILL VERY  
15 COSTLY AND RESOURCE INTENSIVE PROCESS TO DEVELOP  
16 THIS THERAPY WITHIN A SIX-MONTH TIME FRAME.

17 AND SINCE THIS N OF 1 THERAPY WAS  
18 DEVELOPED FOR A SINGLE PATIENT AND TESTED FOR A  
19 SINGLE PATIENT, THE NEXT BABY KJ WOULD REQUIRE THE  
20 ENTIRE PROCESS TO BE REPEATED.

21 SO I'M GOING TO TAKE A QUICK PAUSE HERE  
22 AND GO BACK TO A PREVIOUS SLIDE, AND I'M GOING TO  
23 MAKE AN ANALOGY TO CARS. AND SO I DRIVE A VERY  
24 UTILITARIAN HONDA CRV, AND I'M GOING TO COMPARE THAT  
25 TO A HONDA CIVIC, A SEDAN. SO YOU'VE GOT A CRV,

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1 WHICH IS AN SUV, AND A SEDAN, WHICH IS THE HONDA  
2 CIVIC. NOW, ON THE FACE OF IT, THEY LOOK LIKE TWO  
3 COMPLETELY DIFFERENT CARS WITH DIFFERENT FUNCTIONS  
4 AND DIFFERENT LIFESTYLES THAT THEY WOULD BE TAILORED  
5 TO. HOWEVER, THEY'RE ACTUALLY BASED ON THE SAME  
6 PLATFORM. SO THE CRV WAS DESIGNED AND TESTED AND  
7 MANUFACTURED ON THE CIVIC PLATFORM, AND EVERY  
8 SUCCESSIVE GENERATION IS BUILT ON THE CIVIC PLATFORM  
9 AS WELL. THIS WAS A DELIBERATE STRATEGY TO LEVERAGE  
10 PLATFORM EFFICIENCIES FOR DESIGN, DEVELOPMENT,  
11 TESTING, AS WELL AS MANUFACTURING AND MAINTENANCE OF  
12 THESE TWO MODELS OF CARS FOR EVERY GENERATION.

13 SO WHAT IF FOR DRUG DEVELOPMENT YOU WERE  
14 ABLE TO LEVERAGE TO THE FULL POTENTIAL ALL OF THE  
15 PLATFORM EFFICIENCIES FROM DISCOVERY TO DEVELOPMENT  
16 TO CLINICAL TESTING TO APPROVAL? AND THAT'S THE  
17 BASIS OF WHAT CONSTITUTES THIS CONCEPT OF  
18 PLATFORM-BASED THERAPIES.

19 SO HERE MULTIPLE RELATED THERAPIES FOR  
20 MULTIPLE INDICATIONS ARE RAPIDLY ADVANCED TO  
21 PATIENTS BY LEVERAGING COMMON COMPONENTS,  
22 TECHNOLOGIES, DATA, AND RESOURCES. SO THIS SLIDE  
23 ILLUSTRATES THREE POTENTIAL GENETIC THERAPIES THAT  
24 ARE PLATFORMIZABLE. THIS INCLUDES NONVIRAL GENE  
25 EDITING, RNA-BASED THERAPIES, AND AAV GENE DELIVERY.

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1           NOW, IF WE LOOK AT THE GENE EDITING CRISPR  
2           TECHNOLOGY IN PARTICULAR, CRISPR HAS REVOLUTIONIZED  
3           MEDICINE BECAUSE IN A WAY IT MAKES IT REALLY EASY TO  
4           DISCOVER A LARGE NUMBER OF CANDIDATES FOR MULTIPLE  
5           MUTATIONS. AND THE REASON FOR THIS IS BECAUSE THE  
6           MACHINERY FOR CRISPR OR GENE EDITING INCLUDES AN  
7           EDITOR, WHICH IS GOING TO DO THE MODIFICATION TO THE  
8           DNA, A GUIDE RNA WHICH DIRECTS THE EDITORS TO THE  
9           APPROPRIATE GENETIC SEQUENCE, AND A DELIVERY  
10          VEHICLE, LIKE AN LNP. SO IN THAT INSTANCE, YOU CAN  
11          GENERATE A LARGE NUMBER OF DIFFERENT CANDIDATES  
12          RAPIDLY BY ITERATING JUST ON THE GUIDE RNA.

13                 HOWEVER, WHERE THE CHALLENGE LIES IS HOW  
14          YOU EXTEND THAT PLATFORM EFFICIENCY FROM JUST DRUG  
15          DISCOVERY TO DEVELOPMENT, PRECLINICAL DEVELOPMENT,  
16          CLINICAL TRIALS, AND APPROVAL. AND SO ON THE NEXT  
17          SLIDE I'M GOING TO DEMONSTRATE THE VISION FOR  
18          PLATFORM EFFICIENCIES WHERE YOU CAN LEVERAGE IT  
19          ACROSS THE ENTIRE LIFE CYCLE FOR DRUG DEVELOPMENT.

20                 SO I'M GOING TO GO BACK TO THE BABY KJ  
21          EXAMPLE. SO BABY KJ HAS A UREA CYCLE DISORDER WHICH  
22          AFFECTS ONE PARTICULAR GENE. HOWEVER, THERE ARE SIX  
23          OTHER GENES WHERE A MUTATION IN ANY ONE OF THOSE  
24          GENES CAN RESULT IN THE SAME TYPE OF DISEASE WITH  
25          SIMILAR PATHOLOGY. AND SO WHAT IF YOU WERE TO

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1 DEVELOP GENETIC THERAPIES FOR ALL SEVEN GENES AT THE  
2 SAME TIME IN PARALLEL? AND THAT'S WHAT THIS  
3 PARTICULAR SLIDE IS GOING TO ENCAPSULATE.

4 SO FIRST OF ALL, AS I ALREADY MENTIONED,  
5 YOU CAN RAPIDLY IDENTIFY THERAPIES FOR ALL SEVEN  
6 MUTATIONS IN THIS SIMPLIFIED EXAMPLE BY JUST  
7 CHANGING THE GUIDE RNA SEQUENCE.

8 NEXT, AT THE PRECLINICAL STAGE, IF YOU  
9 RESERVE THE BULK OF THE TESTING ON A SINGLE  
10 CANDIDATE, SO YOU DO ALL OF YOUR ANIMAL TESTING, ALL  
11 OF YOUR SAFETY AND EFFICACY TESTING, ON A SINGLE  
12 CANDIDATE AND YOU RESERVE IN VITRO TESTING FOR THE  
13 REST OF THE CANDIDATES, YOU COULD REALIZE A LOT OF  
14 EFFICIENCY AT THE PRECLINICAL STAGE.

15 AND, IN FACT, THIS APPLIES TO  
16 MANUFACTURING AS WELL WHERE, IF YOU HAVE SIMILAR  
17 COMPONENTS LIKE THE LIPID NANOPARTICLE AND EDITOR,  
18 BY MANUFACTURING AT SCALE ACROSS ALL SEVEN  
19 CANDIDATES, YOU CAN REALIZE THAT EFFICIENCY AS WELL.

20 THE NEXT STEP WOULD BE TO, INSTEAD OF  
21 DOING A SINGLE CLINICAL TRIAL FOR EVERY SINGLE  
22 CANDIDATE DRIVEN BY ITS OWN IND, IS TO SUBMIT A  
23 MASTER PROTOCOL IND TO THE FDA. AND THE FDA WILL  
24 ALLOW YOU TO CONDUCT AN UMBRELLA TRIAL WHERE YOU CAN  
25 STUDY ALL SEVEN OF THOSE CANDIDATES AT THE SAME TIME

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1 IN THE SAME TRIAL WHILE ALSO BEING ABLE TO ADD NEW  
2 CANDIDATES FOR NEW MUTATIONS THAT MAY ARISE IN THAT  
3 PATIENT POPULATION.

4 FINALLY, INSTEAD OF SUBMITTING EVERY  
5 SINGLE CANDIDATE TO THE FDA FOR APPROVAL, WHAT IF  
6 THE FDA ALLOWED YOU TO GET PLATFORM-BASED APPROVAL  
7 FOR THE ENTIRE PLATFORM BASED ON THE TOTALITY OF THE  
8 DATA YOU'VE GATHERED ACROSS ALL THOSE CANDIDATES?  
9 THAT WOULD ALLOW YOU NOT ONLY TO RAPIDLY GET  
10 APPROVAL FOR THIS PLATFORM, BUT TO ALSO GET RAPID  
11 APPROVAL FOR THE NEXT SET OF THERAPIES THAT ALSO  
12 LEVERAGE THAT PLATFORM.

13 AND SO TO DATE THE THOUGHT WAS THAT TO GET  
14 TO THIS VISION FOR PLATFORM-BASED DEVELOPMENT, YOU  
15 HAVE TO MAKE INCREMENTAL STEPS TOWARD EFFICIENCIES.  
16 FOR EXAMPLE, ELIMINATE ONE ANIMAL STUDY HERE OR  
17 REDUCE THE NUMBER OF ANIMAL TESTING IN CERTAIN  
18 AREAS, AND BUILD ON THAT BY ITERATING ON EACH STEP  
19 OF THE PLATFORM TO GET TO THIS VISION. HOWEVER,  
20 THAT HAS CHANGED IN THE LAST YEAR BASED ON SOME  
21 EARLY INDICATIONS.

22 SO FIRST OF ALL, I MENTIONED THE CHOP TEAM  
23 WHICH DEVELOPED THE BABY KJ THERAPY. THEY HAD  
24 STARTED OFF WITH THIS STRATEGY IN MIND, WHICH WAS TO  
25 DEVELOP GENETIC THERAPIES IN PARALLEL FOR ALL SEVEN

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1       MUTATIONS.  AND, IN FACT, THEY'VE GONE TO THE FDA  
2       AND GOTTEN PRE-IND FEEDBACK TO EXECUTE ON THIS  
3       SPECIFIC PLATFORM STRATEGY, WHICH IS TO REALIZE ALL  
4       THE EFFICIENCIES AT THE PRECLINICAL TESTING STAGE  
5       AND TO DO AN UMBRELLA CLINICAL TRIAL FOR ALL SEVEN  
6       GENES AT THE SAME TIME.

7                 IN ADDITION TO THAT, A FEW MONTHS AGO THE  
8       FDA, INSPIRED BY, IN PART, THE BABY KJ EXAMPLE,  
9       ISSUED A PUBLICATION WHERE THEY DESCRIBED THE  
10      PLAUSIBLE MECHANISM PATHWAY.  THIS PATHWAY IS MEANT  
11      TO DRAMATICALLY ACCELERATE DEVELOPMENT AS WELL AS  
12      APPROVAL FOR PLATFORM-BASED GENETIC THERAPIES FOR  
13      RARE DISEASES.  SO WHILE A LOT NEEDS TO STILL BE  
14      DONE IN TERMS OF PROVING THIS PLATFORM APPROACH CAN  
15      BE DONE MULTIPLE TIMES WITH DIFFERENT TYPES OF  
16      CANDIDATES AND DIFFERENT INDICATIONS, TO DEMONSTRATE  
17      CLINICAL PROOF OF CONCEPT AS WELL, AT THIS POINT IN  
18      TIME THERE'S A CLEAR FEEDBACK LOOP BETWEEN THERAPY  
19      DEVELOPERS AS WELL AS REGULATORS ON HOW TO ADVANCE  
20      PLATFORM-BASED GENETIC THERAPY DEVELOPMENT FOR THE  
21      VAST NUMBER OF GENETIC DISEASES THAT AFFECT THE  
22      CURRENT HUMAN POPULATION.

23                 SO I'M GOING TO TAKE A STEP BACK AND TALK  
24      ABOUT HOW WE GOT HERE IN THE LAST YEAR WITH RESPECT  
25      TO THE CHOP ADVANCEMENTS AS WELL AS THE FDA

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1 RECEPTIVITY TO THESE APPROACHES. SO ALL THE WORK  
2 THAT THE CHOP TEAM DID WITH RESPECT TO BABY KJ AS  
3 WELL AS THE BROADER PLATFORM-BASED STRATEGY IS  
4 ENABLED BY A SET OF VISIONARY FUNDING OPPORTUNITIES  
5 THAT THE NIH LAUNCHED THREE YEARS AGO. THEY HAD A  
6 VERY SIMPLE ASK FOR PROPOSALS, WHICH WAS TO BRING TO  
7 THEM AN EFFICIENT WAY OF DEVELOPING MULTIPLE GENETIC  
8 THERAPIES FOR MULTIPLE DISEASES.

9 AT THE SAME TIME, AROUND 2024, THE FDA  
10 ISSUED PLATFORM DESIGNATION DRAFT GUIDANCE. THIS IS  
11 BASED ON REQUIREMENTS OF THE 21ST CENTURY CURES ACT.  
12 HOWEVER, THAT PLATFORM DESIGNATION IS NOT ENTIRELY  
13 USEFUL FOR GENETIC THERAPY DEVELOPERS BECAUSE IT  
14 REQUIRES YOU TO HAVE AN APPROVED PRODUCT IN THE  
15 FIRST PLACE. SO THAT SPURRED A LOT OF DIRECT  
16 ENGAGEMENT BETWEEN THERAPY DEVELOPERS, PATIENT  
17 ADVOCACY ORGANIZATIONS, AND THE GENERAL PUBLIC WITH  
18 THE FDA IN VARIOUS DIFFERENT FORMS, WHICH BY AND  
19 LARGE INFORMED THE PLAUSIBLE MECHANISM PATHWAY.

20 SO AT THIS POINT IN TIME, THE RAPID  
21 FUNDING OPPORTUNITY IS POSITIONED TO ADVANCE  
22 PLATFORM-BASED THERAPIES FROM PROMISE TO PRACTICE BY  
23 BUILDING ROBUST EVIDENCE ACROSS RARE DISEASES AND  
24 TECHNOLOGIES FOR THIS TYPE OF PLATFORM-BASED  
25 APPROACH, TO REALLY GO FORWARD WITH MULTIPLE

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1 THERAPIES FOR MULTIPLE INDICATIONS WHERE YOU REALIZE  
2 PLATFORM EFFICIENCIES AT EVERY STEP OF THE  
3 DEVELOPMENT PROCESS.

4 SO IN DESIGNING THIS PROGRAM, WE HAD TWO  
5 BROAD GOALS. THE FIRST WAS SCIENTIFIC AND  
6 REGULATORY INNOVATION AND THE SECOND WAS PATIENT  
7 IMPACT. FOR THE FORMER, WHAT WE WANTED TO ACHIEVE  
8 WAS THAT BY SUPPORTING MULTIPLE PROJECTS, THAT ALL  
9 OF THEM WOULD DEMONSTRATE THAT YOU CAN GET THIS  
10 PATHWAY REALIZED FOR MULTIPLE TECHNOLOGIES AND  
11 MULTIPLE INDICATIONS AND BUILD AN EVIDENCE BASE FOR  
12 GENE THERAPY PLATFORMS THAT OTHERS CAN LEVERAGE.

13 AT THE SAME TIME ALL OF THIS POTENTIAL IS  
14 NOT REALIZED UNLESS YOU CAN DEMONSTRATE IMPACT ON  
15 THE ACTUAL PATIENTS WHO SUFFER FROM THESE DISEASES.  
16 AND SO THE PROGRAM WOULD HAVE TO ENSURE THAT ANY  
17 SUPPORTED THERAPIES WOULD REACH PATIENTS AS QUICKLY  
18 AS POSSIBLE AND THAT THEY WOULD BLAZE A PATHWAY FOR  
19 OTHERS TO FOLLOW.

20 SO WITH THAT IN MIND, THE RAPID PROGRAM  
21 HAS A SINGLE OBJECTIVE, WHICH IS TO CREATE A  
22 SCALABLE MODEL TO RAPIDLY DELIVER TRANSFORMATIVE,  
23 PLATFORM-BASED GENETIC THERAPIES TO PATIENTS WITH  
24 RARE DISEASE.

25 SO AS YOU KNOW, WE HAVE A SET OF LEGACY

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1 PROGRAMS LIKE TRANSLATIONAL AND CLIN1 AS WELL AS  
2 NEWER PROGRAMS LIKE PDEV AND CLIN2, ALL WHICH  
3 SUPPORT THERAPY DEVELOPMENT BOTH AT THE PRECLINICAL  
4 STAGE AND CLINICAL STAGES. THESE PROGRAMS HAVE A  
5 VAST PORTFOLIO OF RARE DISEASE PROJECTS, AND THEY'LL  
6 CONTINUE TO SUPPORT THOSE GOING FORWARD. HOWEVER,  
7 THESE PROGRAMS ARE NOT CURRENTLY DESIGNED TO  
8 ACCELERATE INNOVATIVE, HIGH-RISK PLATFORM  
9 APPROACHES. WHY IS THAT? BECAUSE THESE PROGRAMS  
10 ARE FOCUSED ON THE TRIED AND TRUE WAY OF DEVELOPING  
11 DRUGS, WHICH IS TO FOCUS A PROJECT ON A SINGLE  
12 CANDIDATE FOR A SINGLE INDICATION THROUGH THE FULL  
13 SUITE OF TESTING FOR EVERY ONE OF THOSE PROJECTS, TO  
14 CONDUCT A CLINICAL TRIAL FOR A SINGLE CANDIDATE  
15 UNDER A SINGLE IND. SO A LOT OF SINGLES THERE.

16 FOR THIS PROGRAM, THE RAPID PROGRAM, THE  
17 INTENT IS TO SUPPORT DEVELOPMENT IN PARALLEL FOR  
18 MULTIPLE CANDIDATES, FOR MULTIPLE RELATED  
19 INDICATIONS, ALL OF WHICH WOULD FEED INTO A MASTER  
20 PROTOCOL TRIAL. AND HERE THE TESTING ON THE  
21 NONCLINICAL SIDE WOULD HAVE TO BE OPTIMIZED WHERE  
22 MOST OF IT IS BEING DONE FOR A LEAD CANDIDATE AND  
23 REDUCED TESTING FOR THE REST OF THOSE CANDIDATES.  
24 AND TO ENSURE ALL THIS HAS PATIENT IMPACT IS TO  
25 CLEAR AN ACCELERATED PATHWAY TO THE CLINIC FOR THESE

1 PROJECTS.

2 SO IN A NUTSHELL, MOVING AWAY FROM SINGLE  
3 CANDIDATES, SINGLE INDICATION, AND SERIAL  
4 DEVELOPMENT OF EACH OF THOSE TO PARALLEL DEVELOPMENT  
5 OF MULTIPLE CANDIDATES WHERE ALL OF THAT IS MADE  
6 EFFICIENT ON THE WORK THAT HAS BEEN DONE SO FAR.

7 SO WITH THAT IN MIND, WE ENVISION TWO  
8 TYPES OF AWARDS FOR THE RAPID PROGRAM. THE FIRST IS  
9 WHAT WE CALL VALIDATION AWARDS. THESE AWARDS ARE  
10 MEANT TO ACCELERATE THOSE PROJECTS THAT HAVE  
11 POSITIVE PRE-IND FEEDBACK FROM THE FDA ON A  
12 PLATFORM-BASED STRATEGY. AND THE INTENT OF THIS IS  
13 TO ACCELERATE THOSE THERAPIES TO CLINICAL PROOF OF  
14 CONCEPT. DEMONSTRATE THAT THE PRECLINICAL  
15 EFFICIENCIES RESULT IN CLINICAL SAFETY AND EFFICACY  
16 FOR THESE PLATFORM-BASED THERAPIES. AND THAT WILL  
17 THEN CREATE A BLUEPRINT FOR OTHERS TO ADVANCE THE  
18 SAME TYPES OF APPROACHES.

19 SO POTENTIAL EXAMPLE PROJECTS, THESE ARE  
20 NONLIMITING, COULD BE NONVIRAL LIVER-TARGETED BASED  
21 EDITING THERAPIES FOR METABOLIC DISORDERS. THEY  
22 COULD BE AAV-BASED GENE THERAPY FOR NEURODEVELOPMENT  
23 DISORDERS. AND THE GOAL -- TO ACHIEVE THE PROGRAM  
24 OBJECTIVE, THESE AWARDS WOULD DEMONSTRATE THAT YOU  
25 CAN REDUCE FROM PROMISE TO PRACTICE THIS

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1 PLATFORM-BASED THERAPY DEVELOPMENT AND THAT YOU CAN  
2 DEVELOP AN EVIDENCE BASE OF CLINICAL SAFETY AND  
3 EFFICACY FOR THESE THERAPIES. YOU CAN DELIVER THESE  
4 THERAPIES TO PATIENTS, AND YOU CAN DEMONSTRATE THEIR  
5 SAFETY AND EFFICACY.

6 SO TO DESCRIBE THE AWARDS IN A LITTLE BIT  
7 MORE DETAIL, THE VALIDATION AWARDS WILL SUPPORT IN  
8 VIVO GENETIC THERAPIES FOR RARE DISEASES WHERE THE  
9 PLATFORM WILL HAVE TO DEMONSTRATE ACCELERATED AND  
10 RESOURCE-EFFICIENT DEVELOPMENT. SO THESE WILL BE  
11 PROGRAMS WHERE THE APPLICANT HAS ALREADY SECURED FDA  
12 FEEDBACK ON THIS PLATFORM-BASED APPROACH, AND THE  
13 PROJECT WILL BE FUNDED TO CONDUCT ALL THE IND  
14 ENABLING STUDIES, SUBMIT THE MASTER PROTOCOL IND,  
15 AND TO CONDUCT THAT MASTER PROTOCOL CLINICAL TRIAL  
16 WITH THE EXPECTED OUTCOME THAT THEY WOULD COMPLETE  
17 THAT TRIAL FOR AT LEAST THREE CANDIDATES.

18 THAT WOULD SET THESE PROJECTS UP TO  
19 POTENTIALLY TAKE ADVANTAGE OF THE FDA'S PLAUSIBLE  
20 MECHANISM PATHWAY, ALLOWS FOR RAPID DEVELOPMENT AS  
21 WELL AS RAPID POTENTIAL PLATFORM APPROVAL FOR THESE  
22 TYPES OF APPROACHES.

23 THESE AWARDS WOULD NOT -- THE PA FOR THIS  
24 PROGRAM WOULD NOT SPECIFY AN AWARD CAP AND WILL NOT  
25 REQUIRE MINIMUM CO-FUNDING. THE REASON FOR THIS IS

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1 TO PUT THE ONUS ON THE APPLICANT TO DEMONSTRATE A  
2 WELL-JUSTIFIED BUDGET THAT REALIZES TIME, COST, AND  
3 RESOURCE EFFICIENCIES ACROSS THE ENTIRE SPECTRUM OF  
4 PRECLINICAL AND CLINICAL DEVELOPMENT. AND BECAUSE  
5 WE ANTICIPATE A VERY BROAD RANGE OF PROJECTS MIGHT  
6 BE ELIGIBLE FOR SUCH A PROGRAM, THAT AN AWARD CAP  
7 WOULD BE LIMITING AND DIFFICULT TO SPECIFY. LIKE  
8 THE PDEV PROGRAM, THIS PROGRAM WOULD BE LIMITED TO  
9 CALIFORNIA ORGANIZATIONS ONLY.

10 THE SECOND TYPE OF AWARD IS A RAPID  
11 INNOVATION AWARD. THE MAIN OBJECTIVE FOR THESE  
12 AWARDS IS TO PUSH THE BOUNDARIES OF WHAT CONSTITUTES  
13 PLATFORMS. SO WE'RE LOOKING HERE FOR INNOVATIVE  
14 REGULATORY AND TECHNOLOGY SOLUTIONS THAT COULD  
15 EXPAND THE PLATFORM CAPABILITIES AND THAT COULD ALSO  
16 EXPAND TO A MUCH BROADER RANGE OF RARE GENETIC  
17 DISEASES. AND WE WOULD SUPPORT THESE PROJECTS  
18 THROUGH ALL OF THE PRECLINICAL ACTIVITIES TO OBTAIN  
19 IND CLEARANCE FOR THAT PLATFORM-BASED APPROACH.

20 SO SOME EXAMPLES OF INNOVATIVE APPROACHES  
21 HERE COULD BE NONVIRAL GENE DELIVERY TECHNOLOGIES  
22 FOR CNS DISORDERS. OR IT COULD BE NEXT GENERATION  
23 GENE EDITING THERAPIES THAT ALSO INCORPORATE NOVEL  
24 IN VITRO MODELS THAT REDUCE THE NEED FOR ANIMAL  
25 TESTING. AGAIN, THESE ARE NONLIMITING EXAMPLES JUST

1 FOR THE SAKE OF ILLUSTRATION.

2 THESE AWARDS WILL ADVANCE THE PLATFORM  
3 GOALS BY DEMONSTRATING THAT NEXT GENERATION  
4 TECHNOLOGIES CAN BE DEVELOPED WITH A PLATFORM  
5 APPROACH IN MIND. AND THEY WOULD ALSO DEMONSTRATE  
6 AN ADVANCEMENT IN REGULATORY STRATEGIES GOING  
7 FORWARD FOR THESE EMERGING PLATFORMS.

8 I'LL BRIEFLY DESCRIBE WHAT THESE AWARDS  
9 MIGHT LOOK LIKE. SO AS I MENTIONED, THE CANDIDATES  
10 HERE WOULD BE IN VIVO GENETIC THERAPIES FOR RARE  
11 GENETIC DISEASES. THE APPLICANT WOULD HAVE TO HAVE  
12 HAD OR REQUESTED AN FDA INTERACT MEETING FOR THEIR  
13 PLATFORM-BASED APPROACH BECAUSE THAT EARLY FDA  
14 INTERACTION IS CRITICAL FOR THESE VERY NOVEL,  
15 HIGH-RISK PROJECTS.

16 THE AWARD WOULD SUPPORT ALL OF THEIR  
17 PRECLINICAL ACTIVITIES TO GET TO A MASTER PROTOCOL  
18 IND FOR AT LEAST THREE CANDIDATES. AND LIKE THE  
19 VALIDATION AWARD, THESE AWARDS WOULD ALSO NOT HAVE A  
20 SPECIFIC AWARD CAP, AND THEY WOULD NOT REQUIRE A  
21 MINIMUM CO-FUNDING REQUIREMENT FOR THE SAME REASONS  
22 THAT I MENTIONED PREVIOUSLY. AND LIKE THE  
23 VALIDATION AWARDS AND THE PDEV PROGRAM, THE  
24 APPLICANTS FOR THE INNOVATION AWARDS WOULD BE  
25 LIMITED TO CALIFORNIA ORGANIZATIONS.

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1 TO SUPPORT THESE TYPES OF PROJECTS, CIRM  
2 REQUESTS FROM THE BOARD TO AUTHORIZE A DEFINED  
3 BUDGET OF A \$100 MILLION FOR TWO ANNUAL FUNDING  
4 CYCLES. AND BECAUSE OF THE DYNAMIC NATURE OF THESE  
5 PROJECTS, CIRM WILL ALSO REQUEST A SUPPLEMENT BUDGET  
6 THAT WILL ALLOW US TO FURTHER ACCELERATE FUNDED  
7 PROJECTS SUBJECT TO A CIRM REQUEST AND APPROVAL  
8 PROCESS. SO THE TABLE BELOW DESCRIBES HOW THE \$100  
9 MILLION WOULD BE DEPLOYED.

10 SO IN FISCAL YEAR 26/27, CIRM WOULD  
11 REQUEST FROM THE BOARD TO AUTHORIZE \$55 MILLION IN  
12 FUNDING FOR THE RAPID PROGRAM. \$50 MILLION OF THIS  
13 ALLOCATION WOULD BE USED TO FUND TWO TO THREE  
14 AWARDS. AND \$5 MILLION OF THIS WOULD BE RESERVED AS  
15 A SUPPLEMENT TO BE DEPLOYED OVER THE LIFETIME OF THE  
16 PROGRAM. THE SUPPLEMENT DETAILS ARE DESCRIBED IN  
17 THE MEMO AND IN THE CONCEPT. I'M HAPPY TO ELABORATE  
18 ON THOSE DURING THE Q AND A IF NEEDED.

19 IN FISCAL YEAR 27/28 WE ANTICIPATE ASKING  
20 THE BOARD TO AUTHORIZE AN ADDITIONAL \$45 MILLION,  
21 ALL OF WHICH WILL BE DEDICATED TOWARD NEW AWARDS,  
22 AND WE ANTICIPATE FUNDING TWO TO THREE AWARDS IN  
23 THAT CYCLE.

24 GIVEN THE DYNAMIC NATURE OF THESE  
25 PROJECTS, IT'S ANTICIPATED THAT FUNDS MAY BE

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1 RECOVERED AS A CONSEQUENCE OF NORMAL AWARD  
2 MANAGEMENT OPERATIONS. AND IF ENOUGH FUNDS ARE  
3 RECOVERED FROM RAPID AWARDS, CIRM MAY REQUEST TO THE  
4 BOARD TO AUTHORIZE ADDITIONAL FUNDING TO OPEN UP A  
5 NEW ROUND OR REPLENISH THE SUPPLEMENT BUDGET. THIS  
6 WOULD BE AS PART OF A RESEARCH BUDGET APPROVAL  
7 PROCESS ON AN ANNUALIZED BASIS.

8 I'M GOING TO SPEND THE NEXT COUPLE OF  
9 SLIDES TALKING ABOUT THE APPLICATION AND REVIEW  
10 PROCESS AS WELL AS SOME OF THE AWARD MANAGEMENT  
11 FUNCTIONS OF THIS PROGRAM. THEY'RE VERY SIMILAR TO  
12 OUR EXISTING PROGRAM, SO I'M NOT GOING TO ELABORATE  
13 TOO MUCH ON THESE POINTS.

14 SO FIRST OF ALL, GIVEN THE UNIQUE NATURE  
15 OF THIS PROGRAM, WE WILL REQUIRE CONSULTATIONS PRIOR  
16 TO SUBMISSION FROM ALL PROSPECTIVE APPLICANTS. THIS  
17 IS MEANT TO HELP ENSURE THE APPLICANTS ARE MEETING  
18 THE PLATFORM SCOPE AND READINESS ELIGIBILITY  
19 REQUIREMENTS AND TO ALSO GIVE THAT ASSURANCE TO THE  
20 APPLICANT BEFORE THEY EMBARK ON WHAT ARE MOST  
21 DEFINITELY GOING TO BE LENGTHY PROPOSALS.

22 THE RAPID PROGRAM WILL UTILIZE EXISTING  
23 APPLICATION AND GWG REVIEW PROCESSES. SO ALL  
24 APPLICANTS WILL BE REQUIRED TO SUBMIT THE COMPLETE  
25 APPLICATION AT THE TIME OF DEADLINE. AND IF

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1 NECESSARY, IF WE HAVE A LARGE AMOUNT OF APPLICATIONS  
2 THAT NEED TO BE REDUCED IN ORDER TO GO TO SCIENTIFIC  
3 REVIEW, THE GRANTS WORKING GROUP WILL CONDUCT A  
4 POSITIVE SELECTION PROCESS SIMILAR TO WHAT WE'VE  
5 DONE IN THE PAST FOR OTHER PROGRAMS.

6 AND LASTLY, LIKE ALL OF OUR CURRENT  
7 PROGRAMS, THE GRANTS WORKING GROUP WILL SCORE THESE  
8 SUBMISSIONS ON A NUMERICAL 1 TO 100 SCORING SYSTEM  
9 TO AID THE ARS IN MAKING FUNDING DECISIONS.

10 ON THE AWARD MANAGEMENT SIDE, WE WILL  
11 UTILIZE EXISTING AWARD MANAGEMENT MECHANISMS TO  
12 ENSURE THAT RAPID PROJECTS ADHERE TO THE PROGRAM  
13 OBJECTIVE AND EXPECTED OUTCOMES. SO GIVEN THE  
14 DYNAMIC NATURE OF THESE PROJECTS AGAIN, WE  
15 ANTICIPATE UPPING OUR PROACTIVE AWARD MANAGEMENT  
16 PRACTICES, HAVING MORE INTERACTION WITH THE AWARDEE,  
17 BEING THERE WHEN THEY HAVE THOSE FDA INTERACTIONS TO  
18 ENSURE THAT WE'RE IN LOCKSTEP WITH THE PROJECT TEAM  
19 ON THE EXECUTION OF THESE PROJECTS.

20 AND LIKE ALL OF OUR PDEV AND CLIN2  
21 PROGRAMS, THE RAPID AWARDS WILL BE DRIVEN BY  
22 PERFORMANCE DRIVEN OPERATIONAL MILESTONE STRUCTURE.  
23 SO ALL THE FUNDS WILL BE DISBURSED UPON SUCCESSFULLY  
24 MEETING THE OM CRITERIA ON A TIMELY MANNER. WE WILL  
25 ALSO USE THE OM'S HERE IN THIS PARTICULAR INSTANCE

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1 TO ENSURE THAT THESE PROJECTS ARE DELIVERING ON THE  
2 PLATFORM EFFICIENCIES AND ALSO DRIVING TOWARD THE  
3 EXPECTED OUTCOME OF CLINICAL VALIDATION FOR MULTIPLE  
4 CANDIDATES.

5 ANY OM DELAYS WILL TRIGGER EVALUATION AND  
6 POTENTIAL ACTION WHICH IS SIMILAR TO OUR EXISTING  
7 PROGRAMS. AND THE NOTICE OF AWARD WILL DEFINE  
8 SUSPENSION EVENTS THAT COULD HALT FUNDING UNTIL  
9 THOSE EVENTS ARE RESOLVED AS ALSO A STANDARD FEATURE  
10 OF OUR EXISTING AWARD MECHANISMS. SO WE'LL LEVERAGE  
11 ALL OF THESE TOOLS TO ENSURE THAT OUR INVESTMENT IN  
12 THESE PROJECTS IS PROTECTED AND THAT WE ARE  
13 EFFECTIVELY DRIVING THEM TOWARD THE EXPECTED  
14 OUTCOME.

15 LASTLY, I WANT TO STRESS A MAJOR COMPONENT  
16 OF THE SUCCESS OF THIS PROGRAM WILL BE BASED ON  
17 TIMELY KNOWLEDGE AND DATA SHARING. SO WE VIEW THIS  
18 AS TWO PARALLEL MECHANISMS. FIRSTLY, WE EXPECT AND  
19 WILL REQUIRE ALL RAPID AWARDEES TO SHARE IN REAL  
20 TIME THEIR STUDY DESIGNS, THEIR DATA, THEIR  
21 RESOURCES, AND THEIR REGULATORY EXPERIENCE AMONG  
22 CIRM AWARDEES. THIS IS INTENDED TO CAPTURE AND  
23 LEVERAGE THE BROAD AMOUNT OF EXPERTISE WITHIN THE  
24 CIRM AWARDEE NETWORK TO HELP NOT ONLY THESE  
25 PROJECTS, BUT ALSO OUR PDEV AND CLIN2 PROJECTS

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1 LEARNED FROM THE SAME EXPERIENCES.

2 AT THE SAME TIME, WITHIN THE AWARD LIFE  
3 CYCLE, WE WILL REQUIRE THESE PROJECTS TO SHARE THEIR  
4 RELEVANT DATA, THEIR STUDY DESIGNS, AND THEIR FDA  
5 INTERACTIONS WITH THE PUBLIC TO ENSURE THAT THESE  
6 PROJECTS ARE ESTABLISHING AND ADVANCING BEST  
7 PRACTICES FOR PLATFORM-BASED THERAPY DEVELOPMENT  
8 GIVEN THE GREAT DYNAMIC NATURE OF DEVELOPMENT RIGHT  
9 NOW FOR GENETIC THERAPIES.

10 GIVEN THE NATURE OF THIS PROGRAM, WE WOULD  
11 LIKE TO HAVE EARLY OUTREACH TO APPLICANTS. SO IF  
12 THE BOARD WERE TO APPROVE THIS CONCEPT THIS MONTH,  
13 WE WILL EMBARK ON AN OUTREACH STRATEGY THAT IS  
14 INTENDED TO PROMOTE RAPID, IS INTENDED TO FACILITATE  
15 DISCUSSIONS ABOUT PLATFORM-BASED APPROACHES, AND TO  
16 FACILITATE COLLABORATIONS AND RESOURCE SHARING SO  
17 THAT APPLICANTS CAN PUT THE BEST PROPOSALS FORWARD  
18 WHEN THE SUBMISSION DEADLINE COMES AROUND FOR THE  
19 RAPID PROGRAM.

20 THIS OUTREACH MAY INCLUDE EARLY  
21 INTERACTIONS WITH PROSPECTIVE APPLICANTS, ENGAGING  
22 WITH EXPERTS AND PATIENT ADVOCACY ORGANIZATIONS, AND  
23 HOLDING FORUMS AND WORKSHOPS THAT CONVENE KEY  
24 STAKEHOLDERS.

25 SO IF THE BOARD WERE TO APPROVE THIS

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1 CONCEPT IN JANUARY, WE WILL WORK TOWARD A MID-YEAR  
2 APPLICATION DEADLINE. AND WE'RE PROJECTING A  
3 NINE-MONTH TIMELINE FROM APPLICATION OVER TO AWARD  
4 START, WHICH WOULD PUT THE RAPID AWARDS, THE FIRST  
5 WAVE OF THOSE, ON TRACK TO START IN THE EARLY PART  
6 OF 2027.

7 SO WITH THAT, IF YOU'VE BEEN KEEPING  
8 COUNT, I'VE PROBABLY SAID RAPID, MULTIPLE, AND  
9 DYNAMIC ABOUT A HUNDRED TIMES. AND I WOULD LIKE, ON  
10 BEHALF OF CIRM, TO REQUEST THAT THE SCIENCE  
11 SUBCOMMITTEE ENDORSE THE PROPOSED RAPID PROGRAM  
12 CONCEPT FOR ICOC APPROVAL WITH AN INITIAL ALLOCATION  
13 OF \$100 MILLION IN THE FIRST TWO FUNDING CYCLES.  
14 THANK YOU.

15 CHAIRMAN FISCHER-COLBRIE: GREAT, SHYAM.  
16 EXCELLENT PRESENTATION.

17 I JUST WANT TO MAKE A FEW COMMENTS. FIRST  
18 OF ALL, THIS RAPID APPROACH IS REALLY A DIRECT  
19 OUTGROWTH OF THE GENERAL EVOLUTION OF THE FDA  
20 REGULATORY PROCESSES THAT HAVE BEEN HEADED TOWARDS  
21 MAKING IMPROVEMENTS IN PARTICULAR IN THE RARE  
22 DISEASE CATEGORY WHICH ARE HIGHLY PROBLEMATIC FROM  
23 THE TRADITIONAL REGULATORY APPROACHES. AND AS YOU  
24 POINTED OUT, THAT WAS ACCELERATED SIGNIFICANTLY WITH  
25 THE BABY KJ EXPERIENCE AND THE DRIVE BY PATIENT

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1 GROUPS TO EFFECT CHANGE.

2 AND SO WHAT THIS IS IS ALMOST A REAL-TIME  
3 RESPONSE FROM CIRM TO LEVERAGE THE CHANGES IN THE  
4 REGULATORY ENVIRONMENT. AND IT'S A REFLECTION OF  
5 THE TEAM'S CLOSENESS WITH THE FDA AND WITH THE  
6 REGULATORY PROCESSES HISTORICALLY TO BE ABLE TO COME  
7 UP WITH A NEW APPROACH AND A NEW PLATFORM FOR  
8 ACCELERATION.

9 AND IT'S IMPORTANT TO NOTE THOSE ARE ALL  
10 KEY CHARACTERISTICS OF MEETING THE CIRM STRATEGIC  
11 ALLOCATION FRAMEWORK. AND THAT IS, TO WIT, IN THREE  
12 AREAS. ONE IS ACCELERATION OF CURES. THE SECOND IS  
13 THE MECHANISMS AND GOALS WITH RESPECT TO THE  
14 STRATEGIC ALLOCATION FRAMEWORK AROUND RARE DISEASE  
15 SOLUTIONS. AND THE THIRD IS FUNCTIONALLY TO  
16 CONTINUE TO BUILD PLATFORM CAPABILITIES THAT HAVE  
17 THE OPPORTUNITY FOR REPLICATION AND THEN IN TURN  
18 POTENTIALLY DRIVE COSTS DOWN AND EXPAND OTHER  
19 ORGANIZATIONS TO GET INTO THESE CRITICAL AREAS.

20 SO I'M VERY IMPRESSED WITH WHAT THE  
21 PROPOSAL IS HERE. AND WITH THAT, I'M ASKING FOR AN  
22 APPROVAL PROCESS HERE. SO DO WE HAVE A PROPOSAL  
23 APPROVAL AND SECOND FOR THIS APPLICATION?

24 VICE CHAIR BONNEVILLE: SO MOVED.

25 DR. MELTZER: SECOND.

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1 CHAIRMAN FISCHER-COLBRIE: SECOND. GREAT.  
2 WHO WAS THE SECOND, JUST TO CONFIRM?

3 DR. MELTZER: CAROLYN.

4 CHAIRMAN FISCHER-COLBRIE: CAROLYN.  
5 GREAT. SO WITH THAT, LET'S OPEN UP FOR DISCUSSION  
6 AND QUESTIONS BY PEOPLE ON THE CALL. AND WE'LL GET  
7 TO SEE IF THERE'S ANY PUBLIC COMMENT AFTER THAT, BUT  
8 ANY QUESTIONS OR COMMENTS FROM THE SCIENCE  
9 SUBCOMMITTEE? IS THAT SHAWNA?

10 DR. STARK: YES, THAT'S RIGHT. SHAUNA  
11 STARK. THANK YOU.

12 I THINK THIS IS A FABULOUS IDEA, A REALLY  
13 INNOVATIVE MODEL. I THINK WE'VE SEEN MORE PLATFORM  
14 TRIALS SHOWING UP. I THINK THIS IS GREAT.

15 I THINK MY QUESTION IS GOING TO COME DOWN  
16 TO THE MONEY. HOW DOES -- WE DON'T HAVE A NUMBER OF  
17 GRANTS ALLOCATED. MY UNDERSTANDING IS THE BUDGET'S  
18 NOT REALLY SET PER PROJECT. SO HOW DOES IT IMPACT  
19 THE OVERALL BUDGET ALLOCATION ACROSS THE PROGRAMS?

20 DR. PATEL: IT'S A GREAT QUESTION.

21 CHAIRMAN FISCHER-COLBRIE: GO AHEAD.

22 DR. PATEL: YES, IT'S A GREAT QUESTION.  
23 SO WHAT WOULD HAPPEN HERE IS THAT IN THE PA IT WOULD  
24 SPECIFY THAT FOR THIS FIRST YEAR THERE'S A \$50  
25 MILLION ALLOCATION AND WE EXPECT TO FUND TWO TO

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1 THREE AWARDS. AND SO THAT WOULD SET THE EFFECTIVE  
2 CAP. SO THE AWARD -- APPLICATIONS WOULD PROPOSE  
3 THEIR BUDGETS. WE DO A BUDGET REVIEW; BUT WHEN THE  
4 APPLICATION REVIEW SUBCOMMITTEE APPROVES THAT AWARD,  
5 THAT WOULD EFFECTIVELY BE THE MAXIMUM AWARD AMOUNT  
6 FOR THAT PROJECT. AND WE WOULD CONTINUE TO DO  
7 ANOTHER BUDGET REVIEW AFTER THAT DURING CONTRACTING,  
8 AND WE MONITOR THOSE BUDGETS OVER TIME.

9 SO EFFECTIVELY WHAT THAT MEANS IS THAT  
10 WHEN IT COMES TO THE BOARD FOR APPROVAL, THESE  
11 PROPOSALS COME TO THE BOARD FOR APPROVAL, THERE WILL  
12 HAVE TO BE DECISIONS MADE ON WHICH ONES CAN BE  
13 FUNDED UP TO THE \$50 MILLION AWARD AMOUNT, TOTAL  
14 AWARD AMOUNT. I'M ANTICIPATING BEING ABLE TO FUND  
15 TWO TO THREE WITH THAT SORT OF AN ALLOCATION. BUT  
16 IT REALLY DEPENDS ON THE QUALITY OF THE PROJECTS,  
17 THE SCALE OF THOSE PROJECTS, AND WHAT THE BOARD  
18 WANTS TO FUND. SO IT COULD BE ONE, IT COULD BE TWO,  
19 IT COULD BE THREE, OR IT COULD BE EVEN MORE.

20 DR. STARK: THANK YOU.

21 CHAIRMAN FISCHER-COLBRIE: PAT.

22 DR. LEVITT: HI, SHYAM. A FEW QUESTIONS.  
23 I'LL START WITH THE DOLLAR AMOUNT. WHAT WAS THE  
24 EVALUATION YOU DID TO COME UP WITH THAT NUMBER? AND  
25 THESE AWARDS, I CAN'T REMEMBER, WHAT'S THE DURATION

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1 THAT YOU ANTICIPATE FOR THESE AWARDS, FOR A SINGLE  
2 AWARD? HOW MANY YEARS?

3 DR. PATEL: YEAH. SO I'LL ADDRESS THE  
4 SECOND QUESTION FIRST. SO FOR THE VALIDATION, IT'S  
5 SIX YEARS. AND THAT'S BASED ON OUR CURRENT TIMELINE  
6 FOR WHAT IT TAKES TO GO FROM A PRE-IND MEETING TO  
7 COMPLETION OF A CLINICAL TRIAL WITHIN OUR EXISTING  
8 PDEV AND CLIN2. WE ANTICIPATE THAT THE BULK OF THAT  
9 WOULD BE THE CLINICAL TRIAL ACTIVITY.

10 FOR THE INNOVATION AWARD, WHICH IS THE  
11 PRECLINICAL SIDE, THOSE WOULD BE 3.5 YEARS BECAUSE  
12 WE'RE EXPECTING THEM TO MOVE A LOT FASTER IN THAT  
13 RANGE.

14 IN TERMS OF HOW WE CAME ABOUT WITH THE  
15 PROGRAM BUDGET, SO WE RAN SOME SIMULATIONS ON TAKING  
16 JUST OUR EXISTING AWARD CAPS FOR PDEV AND CLIN2 AND  
17 APPLYING SOME MULTIPLICATION FACTORS TO THOSE AND  
18 WHERE WE WOULD END UP. AND ALSO LOOKING AT -- IT  
19 WAS DIFFICULT TO GAUGE, BUT GETTING A SENSE OF HOW  
20 MUCH FUNDING HAD GONE INTO, FOR EXAMPLE, THE CHOP  
21 TEAM'S SOMATIC CELL AND GENE EDITING CONSORTIUM  
22 EFFORTS. AND SO REALLY WITHIN THAT RANGE, WE'RE  
23 LOOKING AT PROJECTS THAT MIGHT BE BETWEEN 20 TO \$30  
24 MILLION FOR THAT VALIDATION AND LOWER FOR THE  
25 INNOVATION.

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1           SO WHAT WE WANTED TO DO WAS ENSURE THAT WE  
2           CAN FUND AT LEAST THREE TO FIVE PROJECTS AND HAVE A  
3           BUDGET TO BE ABLE TO DO THAT AND TO ALSO EXPEND THAT  
4           BUDGET OVER TWO YEARS TO REALLY CAPTURE THE  
5           INNOVATION IN THIS DYNAMIC FIELD.

6           DR. LEVITT: BECAUSE THE CHOP TEAM JUST  
7           GOT A NEW NIH AWARD, RIGHT, FOR AFTER THE SUCCESS.  
8           IT'S 14 MILLION FOR FOUR YEARS. THAT'S TOTAL COSTS.  
9           AND, OF COURSE, OUR INDIRECTS THAT WE PAY ARE MUCH  
10          LESS. SO OUR DIRECT COSTS THAT ARE BEING PROPOSED  
11          ARE OBVIOUSLY MUCH LARGER THAN WHAT -- AND I'M NOT  
12          SUGGESTING NIH THESE DAYS IS A FABULOUS STANDARD TO  
13          GO BY. I HAVE LOTS OF QUESTIONS ABOUT THE CURRENT  
14          MAKEUP OF THE FDA AND HOW WE'RE INVOLVED THERE  
15          BECAUSE I DON'T REALLY QUITE UNDERSTAND THE  
16          EXPERTISE THAT THEY HAVE TO ADDRESS THE VARIOUS  
17          PLATFORM PROPOSALS. BUT THAT'S -- I'LL LEAVE THAT  
18          UP TO YOU AND YOUR TEAM TO DECIDE.

19          I GUESS THE OTHER QUESTION I HAVE IS BABY  
20          KJ NEONATE LIVER METABOLIC DISORDER, AND I KNOW THAT  
21          PEOPLE ARE LOOKING AT THAT AND SAYING IT'S GOING TO  
22          APPLY TO ALL RARE DISEASES. WHAT ARE YOUR THOUGHTS  
23          THERE BECAUSE THEY SPENT A LOT OF YEARS STUDYING  
24          UREA CYCLE AND OTHER METABOLIC DISORDERS THAT ARE  
25          SINGLE GENE DISORDERS AND HAVE A HUGE AMOUNT OF

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1 BIOLOGICAL UNDERSTANDING OF THE INDEPENDENCE OF SOME  
2 OF THESE PATHWAYS IN TERMS OF THEIR CAPABILITY OF  
3 BEING CORRECTED THROUGH GENE EDITING. SO WHAT'S  
4 YOUR THOUGHT ABOUT THE DOMAINS IN WHICH THIS IS  
5 GOING TO BE MORE PROBABLY GREATER APPLICATION THAN  
6 IN OTHERS? I'M SURE YOU THOUGHT ABOUT THIS.

7 DR. PATEL: YEAH. SO I THINK IN TERMS OF  
8 GENE EDITING, AND I'LL ALSO ASK MY COLLEAGUES TO  
9 WEIGH IN ON THEIR EXPERIENCE BECAUSE THEY HAVE BEEN  
10 DOING A DEEPER DIVE. SO WITH RESPECT TO GENE  
11 EDITING, YOU'RE RIGHT, THAT IF WE'RE LOOKING AT  
12 NONVIRAL APPROACHES COMING IN, THEY'RE PROBABLY  
13 GOING TO BE TARGETING THE LIVER WHERE THERE IS THE  
14 GREATEST AMOUNT OF DATA RIGHT NOW AND UNDERSTANDING  
15 THOSE DISEASES.

16 IF YOU BROADEN OUT TO, LET'S SAY, SOME BIO  
17 APPROACHES, FOR EXAMPLE, AAV, THERE'S A LOT OF  
18 UNDERSTANDING OF SOME OF THE NEURODEVELOPMENTAL  
19 DISEASES WHERE THE AAV CAN DELIVER THAT VECTOR AND  
20 THAT PAYLOAD TO THE CELLS. AND IN THOSE INSTANCES,  
21 IN OUR OWN PORTFOLIO AND IN SOME OTHER AREAS OUTSIDE  
22 OF OUR PORTFOLIO, THERE HAVE BEEN SOME PLATFORM  
23 EFFICIENCIES REALIZED FOR THAT SORT OF A MECHANISM  
24 WHERE, BECAUSE THE DELIVERY VEHICLE IS THE SAME, YOU  
25 CAN REDUCE A SIGNIFICANT AMOUNT OF ANIMAL TESTING.

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1 BUT IT WOULD HAVE TO BE A PROPOSAL THAT DEMONSTRATES  
2 HOW YOU CAN TAKE A VIRAL VECTOR THAT'S CNS TARGETED  
3 AND REALLY DEMONSTRATE PLATFORM EFFICIENCIES ACROSS  
4 THAT.

5 JIM AND LISA, IF YOU WANT TO ADD ANY OTHER  
6 PROJECTS THAT YOU'VE BEEN LOOKING AT.

7 DR. CAMPANELLI: THE INBORN ERRORS OF  
8 METABOLISM TARGETING THE LIVER ARE OBVIOUS. AND  
9 RIGHT NOW IT'S JUST A POSSIBILITY. SO WE WOULD BE  
10 CONTRIBUTING TO THE ACTUAL INNOVATION OF WHAT THE  
11 FDA IS TALKING ABOUT IN ORDER -- ERRORS OF IMMUNITY  
12 WOULD BE A NEXT STEP VERY MUCH LIKE THE INBORN  
13 ERRORS OF METABOLISM POTENTIALLY. AND THEN THINKING  
14 BROADER, CYSTIC FIBROSIS IS AN AREA THAT MIGHT BE  
15 AMENABLE TO ONE OF THESE APPROACHES, WHICH YOU MIGHT  
16 NOT HAVE THOUGHT OF.

17 DR. LEVITT: RIGHT. AND TO THE CURRENT  
18 PLATFORM, THE CURRENT PLATFORMS, I ASSUME, INCLUDE  
19 COMPONENTS THAT REALLY ADDRESS ISSUES OF, FOR  
20 EXAMPLE, OFF TARGET OR IMMUNOLOGICAL OR THE  
21 POTENTIAL FOR NEGATIVE IMMUNOLOGICAL RESPONSIVENESS,  
22 RIGHT, BECAUSE THOSE ARE TWO AREAS THAT ARE THE RISK  
23 FACTORS, RIGHT. SO I ASSUME THE PLATFORMS WOULD BY  
24 DEFINITION NEED TO INCLUDE WAYS IN WHICH THOSE ARE  
25 IDENTIFIED AS LOW OR NO RISK, RIGHT?

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1 DR. PATEL: YEAH. AND SO, FOR EXAMPLE,  
2 WITH RESPECT TO THE UREA CYCLE DISORDER CANDIDATES,  
3 THE BULK OF THE TESTING ON THE OTHER CANDIDATES IS  
4 FOCUSED ON PRETRIAL TARGET TESTING TO DEMONSTRATE  
5 THE SAFETY PROFILE THERE. SO IT WOULD HAVE TO BE A  
6 RISK-BASED STRATEGY ON WHICH TESTING IS APPLIED TO  
7 THE BASKET OF THOSE THERAPIES AND WHAT'S BEING  
8 RESERVED FOR THE MAIN CANDIDATE.

9 DR. LEVITT: IS THE PROGRAM FLEXIBLE  
10 ENOUGH SO THAT IF YOU GET MORE APPLICATIONS THAN YOU  
11 ANTICIPATED? THERE'S GOING TO BE SOME NUMBER OF  
12 CURRENT CALIFORNIA RESEARCH GROUPS THAT ARE SET UP  
13 TO BE ABLE TO DO THIS AND TAKE ADVANTAGE OF THIS  
14 PROGRAM. IT'S NOT GOING TO BE BROADLY APPLIED,  
15 RIGHT? YOU HAVE TO ALREADY BE PRETTY EXPERT IN THIS  
16 AREA. IS THERE ENOUGH FLEXIBILITY FROM YOUR  
17 PERSPECTIVE TO MODIFY WHAT YOU ARE GOING TO PROVIDE  
18 PER GRANT IF YOU GET EXCITING, REALLY INNOVATIVE  
19 PROPOSALS, AND IT'S MAYBE MORE THAN TWO OR THREE, TO  
20 BE ABLE INCREASE THE POSSIBILITY OF DISCOVERY THAT  
21 WOULD MAKE A BIG DIFFERENCE? BECAUSE PUTTING ALL  
22 OUR EGGS INTO TWO OR THREE GROUPS, I'M SURE THEY'LL  
23 ALL BE GREAT, BUT YOU NEVER KNOW.

24 SO I'M ASKING ABOUT FLEXIBILITY. IN THE  
25 SLIDE DECK IT SAYS TWO TO THREE, BUT YOU MENTION

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1       COULD BE UP TO FIVE. SO THAT INDICATED TO ME THAT  
2       YOU'RE THINKING MORE FLEXIBLY, RIGHT, OR NOT?

3               DR. PATEL: YEAH. SO I THINK OVERALL, IF  
4       WE WERE TO PROJECT OUT THE WHOLE \$100 MILLION, WE  
5       COULD ANTICIPATE FIVE OR SIX PROJECTS IN TOTAL,  
6       RIGHT. BUT THAT'S BASED ON US LOOKING AT OUR  
7       CURRENT AWARD CAPS AND PERFECTING ON THAT. IF  
8       THERE'S SIGNIFICANT EFFICIENCIES REALIZED AND THE  
9       NUMBER OF CANDIDATES ARE NOT HUGE, IT'S POSSIBLE  
10      THAT THEY MIGHT EVEN HAVE SMALLER BUDGETS AND WE  
11      DON'T KNOW.

12              IN ORDER TO, I THINK, ENABLE WHAT YOU ARE  
13      ASKING, BECAUSE THERE'S ALWAYS GOING TO BE THAT  
14      CONSTRAINT OF \$50 MILLION FOR THAT PROGRAM FOR THAT  
15      FISCAL YEAR, THAT WOULD LIMIT HOW MANY WE CAN FUND.  
16      BUT I THINK ONE OF THE THINGS THAT WE ARE GOING TO  
17      ENCOURAGE IN THE PA AND IN OUR DISCUSSIONS WITH THE  
18      APPLICANTS IS TO LEVERAGE ANY RESOURCE SHARING, ANY  
19      IN-KIND SUPPORT, ANY VOLUNTARY CO-FUNDING THAT THEY  
20      CAN GET. AND WE'VE SEEN NOT ONLY IN OUR PROGRAMS,  
21      BUT ALSO IN OUR COLLABORATIONS WITH FNIH ON THE  
22      AGCT, THAT THERE ARE MANY VENDORS AND SERVICE  
23      PROVIDERS THAT FIND WAYS TO DO RISK AND COST SHARING  
24      FOR INNOVATIVE APPROACHES. AND SO IT'S POSSIBLE  
25      THAT ALL THOSE COULD FACTOR IN TO REDUCE THE BUDGET

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1 FOR ANY INDIVIDUAL PROJECT.

2 VICE CHAIR BONNEVILLE: AND, PAT, I THINK  
3 SOMETHING TO CONSIDER IS IN THE NEXT ALLOCATION, IF  
4 THE BOARD FEELS THAT MORE MONEY NEEDS TO BE  
5 ALLOCATED TO THIS PROGRAM, THERE IS THE OPPORTUNITY  
6 IN THE BUDGET CYCLE TO DO SO IF THAT'S THE  
7 RECOMMENDATION FROM THE TEAM.

8 DR. LEVITT: OKAY. THANK YOU.

9 CHAIRMAN FISCHER-COLBRIE: ARE THERE OTHER  
10 QUESTIONS? I'M NOT ABLE TO SEE ALL THE HANDS. SO I  
11 DON'T KNOW IF THERE'S OTHER QUESTIONS OR COMMENTS.

12 MR. TOCHER: IT DOESN'T APPEAR SO AT THE  
13 MOMENT.

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

16 MR. TOCHER: IT DOESN'T APPEAR SO, MARK.

17 CHAIRMAN FISCHER-COLBRIE: OKAY. SCOTT,  
18 WITH THAT, IF YOU CALL THE ROLL ON THE VOTE.

19 MR. TOCHER: SURE. MARIA BONNEVILLE.

20 VICE CHAIR BONNEVILLE: YES.

21 MR. TOCHER: DEBORAH DEAS.

22 DR. DEAS: YES.

23 MR. TOCHER: MARK FISCHER-COLBRIE.

24 CHAIRMAN FISCHER-COLBRIE: YES.

25 MR. TOCHER: ELENA FLOWERS.

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1 DR. FLOWERS: YES.  
2 MR. TOCHER: JUDY GASSON.  
3 DR. GASSON: YES.  
4 MR. TOCHER: VITO IMBASCIANI.  
5 CHAIRMAN IMBASCIANI: YES.  
6 MR. TOCHER: PAT LEVITT.  
7 DR. LEVITT: YES.  
8 MR. TOCHER: SHLOMO MELMED.  
9 DR. MELMED: YES.  
10 MR. TOCHER: CAROLYN MELTZER. CHRIS  
11 MIASKOWSKI.  
12 DR. MIASKOWSKI: YES.  
13 MR. TOCHER: SHAUNA STARK.  
14 DR. STARK: YES.  
15 MR. TOCHER: KAROL WATSON.  
16 DR. WATSON: YES.  
17 MR. TOCHER: KEITH YAMAMOTO. GREAT.  
18 THANK YOU. AND THE MOTION CARRIES.  
19 CHAIRMAN FISCHER-COLBRIE: GREAT. THANK  
20 YOU. WITH THAT, LET'S PROCEED TO THE NEXT ITEM ON  
21 THE AGENDA. AND DR. ROSA CANET-AVILES IS GOING TO  
22 PRESENT ON THE PREFERENCES.  
23 DR. CANET-AVILES: MR. FISCHER-COLBRIE,  
24 THE CHAIRS OF THE SCIENCE SUBCOMMITTEE AND THE NEURO  
25 TASK FORCE, DR. PAT LEVITT AS WELL AND DR. CAROLYN

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1 MELTZER, AS WELL AS THE MEMBERS OF THE SCIENCE  
2 SUBCOMMITTEE, AND THE PUBLIC.

3 SO THE PRESENTATION THAT I'M GOING TO SHOW  
4 TODAY, JUST AS AN UPDATE, HAS A FEW -- A LITTLE  
5 ADDITIONAL CONTENT, AND WE WILL REPOST THE MATERIAL  
6 FOR THE ICOC ONCE WE HAVE THE DISCUSSION. THESE  
7 REFINEMENTS HAVE BEEN MADE IN RESPONSE TO SOME BOARD  
8 MEMBER QUESTIONS AFTER WE POSTED LAST WEEK.

9 SO I WOULD LIKE TO START BY TAKING A STEP  
10 BACK AND EXPLAINING WHY WE ARE BRINGING THIS  
11 CONVERSATION TO THE SUBCOMMITTEE TODAY. OVER THE  
12 LAST YEAR AS WE LAUNCHED THE NEW PROGRAM CONCEPTS  
13 AND THE PROGRAM ANNOUNCEMENTS, WE INTRODUCED  
14 PREFERENCES AS PART OF A BROADER EFFORT TO HELP CIRM  
15 TRANSLATE PUBLIC INVESTMENT INTO MEANINGFUL PATIENT  
16 IMPACT WITHIN THE FINITE TIME FRAME THAT WE HAVE.

17 AND SINCE THEN WE HAVE NOW COMPLETED IN  
18 SOME CASES UP TO TWO FUNDING CYCLES. FOR PDEV AND  
19 CLIN2 WE'VE ALREADY DONE TWO CYCLES OF  
20 PRESUBMISSIONS. THUS FAR WE'VE DONE ONE. AND THIS  
21 GAVE US AN OPPORTUNITY TO PAUSE AND LOOK AT HOW THIS  
22 APPROACH IS WORKING IN PRACTICE.

23 THE PURPOSE OF TODAY'S DISCUSSION AND  
24 PRESENTATION IS TO MAKE SURE THAT WE ARE ALL  
25 ANCHORED IN THE SAME UNDERSTANDING OF WHAT THE

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1 PREFERENCES WERE INTENDED TO DO, HOW THEY HAVE BEEN  
2 APPLIED ALONGSIDE SCIENTIFIC REVIEW, AND WHAT ARE  
3 THE EARLY SIGNALS THAT WE ARE STARTING TO SEE.  
4 SOMETIMES THE DATA IS STILL TOO LIMITED TO DRAW  
5 CONCLUSIONS, BUT WE ARE GOING TO PRESENT WHAT WE  
6 HAVE. AND ONE THEME THAT HAS COME UP REPEATEDLY IN  
7 CONVERSATIONS IS THE IMPORTANCE OF KEEPING  
8 PREFERENCES FROM BECOMING TOO RESTRICTIVE.

9 SO THE INTENT OF THE PREFERENCES, JUST TO  
10 CLARIFY, IS TO GUIDE PRIORITIZATION, NOT TO NARROW  
11 THE SCIENCE OR TO EXCLUDE NOVEL IDEAS -- AND WE CAN  
12 GO INTO THIS -- OR TO REPLACE PEER REVIEW. ALL OF  
13 OUR PROGRAMS ARE STILL OPEN, AND SCIENTIFIC QUALITY  
14 AND READINESS CONTINUE TO BE FOUNDATIONAL.

15 SO TODAY'S PRESENTATION IS REALLY A  
16 FRAMING AND LEARNING DISCUSSION. WE WILL WALK  
17 THROUGH THESE EARLY SIGNALS, SHARE WHAT WE THINK WE  
18 ARE SEEING, AND THEN HEAR FROM YOU ABOUT WHAT  
19 ADDITIONAL PORTFOLIO LEVEL ANALYSIS COULD BE MOST  
20 HELPFUL BEFORE WE COME BACK IN MARCH FOR A DEEPER  
21 CONVERSATION ABOUT REFINEMENT FOR OUR FISCAL YEAR  
22 26/27. NEXT SLIDE. AND THANK YOU, LIZ, FOR PASSING  
23 THE SLIDES.

24 SO TODAY'S PRESENTATION, AS I WAS SAYING,  
25 IS A CHECKPOINT, AN OPPORTUNITY TO ALIGN ON

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1 UNDERSTANDING, BRING UP QUESTIONS, AND MAKE SURE WE  
2 ARE ASKING FOR THE ANALYSIS THAT WILL BEST SUPPORT  
3 THOUGHTFUL DECISIONS BY THIS SUBCOMMITTEE AND THE  
4 BOARD LATER ON IN MARCH.

5 SO THIS SLIDE IS MEANT TO GROUND THE REST  
6 OF THE DISCUSSION IN THE OPERATING REALITY THAT WE  
7 ARE WORKING WITHIN. PROP 14 SIGNIFICANTLY EXPANDED  
8 OUR MANDATE BOTH IN TERMS OF SCIENTIFIC CONDITION  
9 AND EXPECTATIONS AROUND PATIENT IMPACT. IN  
10 PARTICULAR, IT REINFORCED PRIORITIES AROUND THE  
11 CENTRAL NERVOUS SYSTEM AND MADE ACCESS AND  
12 AFFORDABILITY AN EXPLICIT PART OF OUR  
13 RESPONSIBILITY, NOT JUST SOMETHING TO CONSIDER  
14 DOWNSTREAM.

15 AT THE SAME TIME, OUR FUNDING REMAINS  
16 FINITE AND TIME BOUND. WE HAVE DEFINED  
17 REMAINING -- WE HAVE A DEFINED REMAINING RUNWAY, AND  
18 THE VOLUME OF SCIENTIFIC STRONG APPLICATIONS WE'VE  
19 RECEIVED CONSISTENTLY EXCEEDS WHAT WE CAN SUPPORT.  
20 THIS IS NOT A REFLECTION OF A DECLINE IN QUALITY.  
21 IT IS A REFLECTION OF DEMAND OUTPACING CAPACITY, AND  
22 IT IS NOT UNIQUE TO CIRM. IT HAPPENS IN ALL FUNDING  
23 AGENCIES.

24 SO TAKEN TOGETHER, THESE TWO REALITIES  
25 CREATE THE CENTRAL TENSION THAT WE ARE TRYING TO

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1 MANAGE, WHICH IS EXPANDED EXPECTATIONS FOR IMPACT  
2 WITHIN FIXED RESOURCES AND A FINITE TIME FRAME. THE  
3 GOAL, THEREFORE, IS NOT SIMPLY TO FUND EXCELLENT  
4 SCIENCE, BUT TO TRANSLATE PUBLIC INVESTMENT INTO  
5 THERAPIES THAT CAN REALISTICALLY REACH PATIENTS  
6 WITHIN OUR LIFETIME, INCLUDING CONSIDERATION OF  
7 FEASIBILITY, READINESS, AND DOWNSTREAM ACCESS.

8 THE BOARD APPROVED A STRATEGIC FRAMEWORK  
9 AND IMPACT GOALS AS THE ROADMAP TO ACHIEVE THAT BACK  
10 IN SEPTEMBER OF 2024. SO PREFERENCES ARE THE  
11 MECHANISM THAT WE'VE INTRODUCED TO HELP NAVIGATE  
12 THIS CHALLENGE. NOT A SUBSTITUTE OF SCIENTIFIC  
13 REVIEW, BUT IS A WAY TO FOCUS LIMITED RESOURCES  
14 TOWARDS THE HIGHEST LIKELIHOOD OF MEANINGFUL PATIENT  
15 THERAPY.

16 SO THE REST OF THE PRESENTATION IS GOING  
17 TO BUILD FROM THIS REALITY. HOW WE ATTEMPTED TO  
18 OPERATIONALIZE PRIORITIZATION, WHAT ARE THE EARLY  
19 SIGNALS THAT WE ARE SEEING, AND WHERE FURTHER  
20 ANALYSIS IS NEEDED BEFORE CONSIDERING ANY  
21 REFINEMENT. AND THEN IN MARCH WE CAN CONSIDER THE  
22 REFINEMENTS.

23 SO STARTING FROM THAT REALITY, WHICH IS  
24 THIS EXPANDED MANDATE, FINITE RESOURCES, AND A  
25 LIMITED RUNWAY, THE PRACTICAL QUESTION HERE BECOMES

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1 HOW DO WE MOVE FROM MANY STRONG APPLICATIONS TO A  
2 PORTFOLIO THAT HAS THE HIGHEST LIKELIHOOD OF  
3 DELIVERING REAL PATIENT IMPACT WITHIN CIRM'S  
4 LIFETIME. AND WE ARE GOING TO DEFINE ALL OF THIS.  
5 NEXT SLIDE.

6 THIS SLIDE SHOWS THE ROLE THAT PREFERENCES  
7 ARE INTENDED TO PLAY, NOT AS A SUBSTITUTE OF  
8 SCIENTIFIC REVIEW, BUT AS A WAY TO FOCUS LIMITED  
9 RESOURCES TOWARDS APPLICATIONS MOST ALIGNED WITH THE  
10 IMPACT GOALS THAT WE DEFINED. ON THE LEFT WE START  
11 WITH A LARGE POOL OF APPLICATIONS. MANY OF THESE  
12 ARE SCIENTIFICALLY STRONG, BUT THEY DRIVE IN TERMS  
13 OF READINESS, FEASIBILITY, ALIGNMENT WITH THE  
14 STATUTORY MANDATES, AND THE LIKELIHOOD OF  
15 TRANSLATING INTO THERAPIES WITHIN THE TIME FRAME  
16 THAT WE HAVE.

17 THE STARS REPRESENT APPLICATIONS THAT MOST  
18 ALIGN WITH OUR GUIDING PRINCIPLES INCLUDING,  
19 CLINICAL IMPACT, FEASIBILITY, ACCESS AND  
20 AFFORDABILITY CONSIDERATIONS, AND RELEVANCE TO OUR  
21 MANDATES. IMPORTANTLY, THE ABSENCE OF A STAR  
22 DOESN'T MEAN THAT THERE IS NO SCIENTIFIC MERIT OR  
23 THAT THE PROPOSAL IS NOT STRONG. IT ONLY REFLECTS  
24 THAT IT HAS LESS ALIGNMENT WITH THESE SPECIFIC  
25 IMPACT-ORIENTED CRITERIA.

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1                    PREFERENCES HELP ENRICH THE POOL BY  
2 BRINGING FORWARD APPLICATIONS THAT ARE MORE LIKELY  
3 TO CONTRIBUTE TO NEAR AND MIDTERM IMPACT GIVEN OUR  
4 CONSTRAINTS. THAT ENRICHED POOL THEN MOVES INTO  
5 SCIENTIFIC AND TECHNICAL REVIEW WHERE THE MERIT, THE  
6 RIGOR, AND THE READINESS ARE EVALUATED IN DEPTH.  
7 THE KEY POINT IS THAT PREFERENCES SHAPE WHICH  
8 APPLICATIONS RISE FOR REVIEW WHILE THE PEER REVIEW  
9 DETERMINES WHICH OF THOSE ARE ULTIMATELY FUNDED.  
10 THIS ALLOWS CIRM TO BOTH UPHOLD THE SCIENTIFIC  
11 EXCELLENCE AND MAKE DELIBERATE CHOICES ABOUT HOW  
12 PUBLIC FUNDS ARE DEPLOYED TO ACHIEVE OUR GOALS.

13                    I WANT TO PAUSE HERE, THIS IS IMPORTANT,  
14 AND ACKNOWLEDGE WHAT WE'VE BEEN HEARING BECAUSE THIS  
15 FEEDBACK IS AN IMPORTANT PART OF WHY WE ARE HAVING  
16 TODAY'S DISCUSSION. SOME OF THE CONCERNS REFLECT  
17 UNCERTAINTY ABOUT HOW PREFERENCES, PRESUBMISSION,  
18 QUALIFICATION INTERACTS WITH SCIENTIFIC REVIEW AND  
19 WHETHER THE PROPOSALS THAT DID NOT ADVANCE WERE  
20 FULLY CONSIDERED ON SCIENTIFIC GROUNDS.

21                    OTHER CONCERNS REFLECT QUESTIONS ABOUT  
22 WHETHER PREFERENCES MIGHT UNINTENTIONALLY FAVOR  
23 CERTAIN MODALITIES OR PATHWAYS OR WHETHER  
24 PROGRESSION WITHIN THE CIRM PORTFOLIO IS BEING  
25 APPROPRIATELY RECOGNIZED.

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1 WE'VE ALSO HEARD A DESIRE FOR GREATER  
2 CLARITY AROUND HOW QUALIFICATION SCORING,  
3 PREFERENCES, AND INTENT FIT TOGETHER AND WHAT  
4 PREFERENCES ARE DESIGNED TO DO VERSUS WHAT THEY ARE  
5 NOT DESIGNED TO DO. MORE IMPORTANTLY, A LOT OF THIS  
6 FEEDBACK IS LESS ABOUT DISAGREEMENT WITH THE GOALS  
7 AND MORE ABOUT UNDERSTANDING THE LOGIC; IN OTHER  
8 WORDS, HOW THE PIECES FIT TOGETHER, HOW DECISIONS  
9 ARE SEQUENCED, AND HOW THIS ULTIMATELY CONNECTS TO  
10 DELIVERING THERAPIES FOR PATIENTS.

11 THAT FEEDBACK HAS HELPED US, AND IT HAS  
12 HELPED US RECOGNIZE THAT WE NEED TO BE MORE CLEAR  
13 AND MORE EXPLICIT IN HOW WE COMMUNICATE THE  
14 RATIONALE BEHIND THESE CHOICES AND ALSO IN HOW WE  
15 SHOW THE LINK BETWEEN PRIORITIZATION DECISIONS AND  
16 IMPACT AND ALSO ABOUT THE FACT THAT, IF WE WANT TO  
17 MAKE AN IMPACT WITH THE CONSTRAINTS THAT WE HAVE OF  
18 FUNDING AND TIME, WE NEED TO MAKE SOME HARD CHOICES.

19 TAKING THAT ALL THAT TOGETHER, THIS  
20 CONTEXT THAT WE ARE OPERATING WITHIN, THE ROLE OF  
21 THE PREFERENCES, AND THE FEEDBACK, THIS BRINGS US TO  
22 WHAT WE ARE TRYING TO ACCOMPLISH IN TODAY'S  
23 DISCUSSION, WHICH IS IN THE NEXT SLIDE.

24 SO THE PURPOSE OF TODAY IS NOT TO DEBATE  
25 INDIVIDUAL OUTCOMES OR TO MAKE DECISIONS ABOUT

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1 PENDING PREFERENCES. IT'S FOCUSED ON THESE THREE  
2 OBJECTIVES. FIRST, WE WANT TO WALK BACK THROUGH THE  
3 RATIONALE FOR THE PREFERENCES, HOW THEY CONNECTED TO  
4 PROPOSITION 14, TO THE STRATEGIC ALLOCATION  
5 FRAMEWORK, AND TO THE PRACTICAL CONSTRAINTS WE ARE  
6 WORKING WITHIN.

7 SECOND, WE WANT TO SHARE WHAT WE HAVE BEEN  
8 LEARNING FROM THE FIRST ROUND OF CYCLES OF  
9 PRE-PREFERENCE APPLICATIONS, THE PRESUBMISSIONS, FOR  
10 PDEV AND CLIN2 AND DISC4. AND THOSE ARE EARLY  
11 SIGNALS. THEY'RE NOT CONCLUSIONS, BUT THEY HELP US  
12 UNDERSTAND WHETHER THE APPROACH IS FUNCTIONING IN  
13 THE WAY THAT IT WAS INTENDED.

14 AND THIRD, WE WANT TO USE THIS COMMITTEE'S  
15 PERSPECTIVE TO IDENTIFY WHAT PORTFOLIO LEVEL  
16 ANALYSES ARE NEEDED BEFORE WE COME BACK IN MARCH TO  
17 HAVE A MORE SUBSTANTIVE DISCUSSION ABOUT REFINEMENT.

18 JUST TO CLARIFY, THE LAST SLIDE SHOWS SOME  
19 OF THE PORTFOLIO ANALYSIS ALREADY THAT HAVE BEEN  
20 SUGGESTED BY BOARD MEMBERS THROUGH PRE-CALLS, AND WE  
21 WILL DISCUSS THOSE, AND THEN THE BOARD CAN DECIDE  
22 WHETHER THEY WANT TO ADD MORE.

23 SO FRAMING TODAY THIS WAY ALLOWS US TO  
24 STAY FOCUSED ON LEARNING AND ALIGNMENT NOW SO THAT  
25 ANY FUTURE DECISIONS ARE GROUNDED IN SHARED

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1 UNDERSTANDING AND DATA. NEXT SLIDE.

2 WITH THAT FRAMING, BEFORE WE GET INTO ANY  
3 SPECIFIC PREFERENCES OR SCORING MECHANICS, IT'S  
4 IMPORTANT TO STEP BACK AND MAKE EXPLICIT THE  
5 PRINCIPLES THAT GUIDED HOW PREFERENCES WERE  
6 DEVELOPED IN THE FIRST PLACE. THESE PRINCIPLES ARE  
7 NOT THEORETICAL. THEY ARE THE BACKBONE OF HOW WE  
8 DESIGNED THE PRECLINICAL AND THE CLINICAL AND THE  
9 PROGRAMS AS WELL AS THE BROADER PORTFOLIO UNDER THE  
10 STRATEGIC ALLOCATION FRAMEWORK. THEY REFLECT THE  
11 REALITIES THAT WE'VE LEARNED OVER YEARS OF FUNDING  
12 THAT EITHER DID OR DIDN'T TRANSLATE INTO THERAPIES  
13 THAT REACHED PATIENTS.

14 SO THE FIRST ONE IS OFFERING POTENTIAL FOR  
15 TRANSFORMATIVE CLINICAL IMPACT. WHAT DO WE MEAN BY  
16 THAT? WHEN WE TALK ABOUT CLINICAL IMPACT, WE ARE  
17 NOT USING IT AS A SYNONYM FOR SCIENTIFIC NOVELTY OR  
18 DISEASE IMPORTANCE. IN THE CONTEXT OF PRECLINICAL  
19 DEVELOPMENT AND CLIN2, CLINICAL IMPACT MEANS THAT  
20 THERE IS A REALISTIC POTENTIAL FOR A THERAPY TO  
21 MEANINGFULLY CHANGE OUTCOMES FOR PATIENTS; THAT IS,  
22 IN TERMS OF EFFICACY, DURABILITY, SAFETY, OR BURDEN  
23 OF CARE COMPARED TO WHAT EXISTS OR POTENTIALLY IS  
24 COMING IN THAT POOL OF APPLICATIONS OR  
25 PRESUBMISSIONS.

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1           THIS PRINCIPLE FORCES US TO ASK NOT  
2           WHETHER THE SCIENCE IS INTERESTING, BUT IF THIS  
3           WORKS, DOES IT ACTUALLY MATTER FOR PATIENTS. THIS  
4           IS JUST ONE PRINCIPLE. WE WILL GET TO OTHERS THAT  
5           DO TAKE INTO ACCOUNT THE SCIENCE.

6           THE SECOND ONE IS THAT IT ADDRESSES  
7           BOTTLENECKS TO ACCESS, AFFORDABILITY, AND  
8           TRANSLATIONAL FEASIBILITY. THIS PRINCIPLE REFLECTS  
9           ONE OF THE MOST IMPORTANT LESSONS EMBEDDED IN THE  
10          SAF, WHICH ARE THAT EARLY DECISIONS AFFECT  
11          DOWNSTREAM ACCESS. AND WE'VE BEEN WORKING ON THIS  
12          UNDER THE UMBRELLA OF THE ACCESSIBILITY AND  
13          AFFORDABILITY WORKING GROUP AND ITS LEADERSHIP.

14          IN BOTH PDEV AND CLIN2, WE HAVE SEEN THAT  
15          CHOICES AROUND MODALITY, DELIVERY, MANUFACTURING  
16          STRATEGY, AND CLINICAL IMPLEMENTATION CAN MAKE THE  
17          DIFFERENCE BETWEEN A THERAPY THAT'S TECHNICALLY  
18          SUCCESSFUL AND ONE THAT IS ACTUALLY USABLE AT SCALE.  
19          SO THIS PRINCIPLE IS NOT ABOUT PRICING POLICY OR  
20          REIMBURSEMENT MANDATES. IT'S ABOUT WHETHER THE  
21          PROPOSED APPROACH ACKNOWLEDGES AND BEGINS TO ADDRESS  
22          NON-BOTTLENECKS, FOR EXAMPLE, OVERLY COMPLEX  
23          MANUFACTURING OR UNREALISTIC DELIVERY ASSUMPTIONS.  
24          PREFERENCES TIED TO SCALABLE MODALITIES AND FEASIBLE  
25          DELIVERY PATHS ARE DIRECT EXPRESSIONS OF THIS

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1 PRINCIPLE.

2 THE THIRD ONE IS THAT IT FILLS CRITICAL  
3 FUNDING GAPS AND ADVANCES CIRM'S STATUTORY MANDATES.  
4 CIRM'S ROLE IS NOT TO FUND EVERYTHING. IT'S TO FUND  
5 WHAT OTHERS CANNOT OR WILL NOT, IN PART. AND THIS  
6 PRINCIPLE REFLECTS THE REALITY THAT CERTAIN DISEASE  
7 AREAS AND MODALITIES OR STAGES OF DEVELOPMENT ARE  
8 PERSISTENTLY UNDERFUNDED BY FEDERAL AGENCIES OR THE  
9 PRIVATE SECTOR DESPITE THEIR POTENTIAL IMPORTANCE.  
10 IN PDEV, FOR EXAMPLE, THIS SHOWS UP HOW WE THINK  
11 ABOUT ENABLING TRANSLATIONAL WORK THAT COULD  
12 OTHERWISE STALL. IN CLIN2 IT SHOWS UP SUPPORTING  
13 TRIALS THAT CARRY SCIENTIFIC OPERATIONAL RISK, BUT  
14 ALIGN STRONGLY WITH OUR MISSION. AND THIS PRINCIPLE  
15 ALSO EXPLICITLY INCORPORATES PROP 14 MANDATES,  
16 INCLUDING THE CNS AND THE PLURIPOTENT STEM  
17 CELL-BASED APPROACHES AS PART OF OUR PRIORITIZATION  
18 LOGIC.

19 THE FOURTH PRINCIPLE IS CAN REALISTICALLY  
20 ACHIEVE KEY REGULATORY AND DEVELOPMENT PATH WITHIN  
21 CIRM'S FINITE RUNWAY? THIS PRINCIPLE IS ONE OF THE  
22 HARDEST AND ALSO ONE OF THE MOST IMPORTANT. IT  
23 DOESN'T MEAN THAT AMBITIOUS SCIENCE IS DISCOURAGED.  
24 IT MEANS THAT WE HAVE TO BE HONEST ABOUT TIMELINES,  
25 DEPENDENCIES, AND WHAT FUNDING -- CIRM FUNDING CAN

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1 REASONABLY ENABLE WITHIN THE YEARS THAT WE HAVE  
2 LEFT.

3 IN CLIN2 THIS IS WHERE READINESS,  
4 REGULATORY CLARITY, AND OPERATIONAL FEASIBILITY  
5 MATTERS SO MUCH. IN PDEV THIS IS WHY THE FOCUS ON  
6 WHETHER A PROGRAM IS POSITIONED TO MAKE A MEANINGFUL  
7 REFLECTION SUCH AS ENABLING AN IND RATHER THAN  
8 ACCUMULATING MORE EXPLORATORY DATA IS COUNTED AS.  
9 THIS PRINCIPLE PROTECTS US BOTH, CIRM AND THE  
10 APPLICANTS, FROM INVESTING HEAVILY IN PROGRAMS THAT,  
11 EVEN IF SCIENTIFICALLY SOUND, ARE UNLIKELY TO REACH  
12 MEANINGFUL MILESTONES WITHIN OUR LIFETIME.

13 THE FIFTH PRINCIPLE IS THAT IT ADDRESSES  
14 DISEASES AFFECTING CALIFORNIANS. AS A PUBLIC  
15 FUNDING AGENCY OF CALIFORNIA, CIRM HAS A  
16 RESPONSIBILITY TO ENSURE THAT OUR PORTFOLIO REFLECTS  
17 DISEASES AND CONDITIONS THAT MEANINGFULLY AFFECT  
18 CALIFORNIANS. THIS DOESN'T MEAN FUNDING ONLY COMMON  
19 DISEASES, NOR DOES IT EXCLUDE RARE DISEASES. WHAT  
20 IT MEANS IS IT REQUIRES US TO BE THOUGHTFUL ABOUT  
21 THE OVERALL BALANCE OF THE PORTFOLIO AND THE  
22 POPULATIONS ULTIMATELY SERVED. AND IT REINFORCES  
23 THE PUBLIC ACCOUNTABILITY DIMENSION OF THE STRATEGY  
24 THAT WE HAVE AND HELPS ENSURE THAT OUR INVESTMENT  
25 STRATEGY REMAINS ALIGNED WITH THE VOTERS' INTENT.

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1                   AND LASTLY, WE HAVE THE PRINCIPLE OF  
2                   DIVERSIFYING CIRM'S ACTIVE AWARD PORTFOLIO. THIS  
3                   FINAL PRINCIPLE IS ACTUALLY VERY IMPORTANT GIVEN THE  
4                   CONCERNS THAT HAVE BEEN RAISED ABOUT PREFERENCES  
5                   BECOMING RESTRICTIVE. DIVERSIFICATION IS A  
6                   GUARDRAIL. IT EXISTS TO PREVENT OVERCONCENTRATION  
7                   IN A SINGLE DISEASE AREA OR MODALITY OR DEVELOPMENT  
8                   PATHWAY EVEN IF THAT AREA IS POPULAR OR WELL  
9                   REPRESENTED AMONG APPLICATIONS. IN PRACTICAL TERMS,  
10                  THIS PRINCIPLE IS WHY THE NOVELTY UNDERREPRESENTED  
11                  DISEASE AREAS RELATIVE TO THE ACTIVE PORTFOLIO ARE  
12                  EXPLICITLY CONSIDERED IN PDEV AND CLIN2 SCORING AT  
13                  DIFFERENT STAGES. IT IS ALSO WHY PREFERENCES ARE  
14                  NOT BINARY GATES. THIS PRINCIPLE ENSURES THAT  
15                  GENUINELY NOVEL OR NON-OBVIOUS APPROACHES, INCLUDING  
16                  OUTLIERS, HAVE A PATHWAY FORWARD RATHER THAN BEING  
17                  COUNTED OUT BY PROGRAMS THAT SIMPLY ALIGN WITH THE  
18                  MOST COMMON PREFERENCES. AND AS I SAID, THEY ARE  
19                  CONSIDERED AT DIFFERENT STAGES IN THE PRESUBMISSION  
20                  OR QUALIFICATION PROCESS.

21                         WITH THOSE GUIDING PRINCIPLES IN MIND, I  
22                         AM GOING TO NOW SHOW HOW THEY WERE TRANSLATED INTO A  
23                         PRACTICAL, PROGRAM-SPECIFIC PREFERENCE RUBRIC. AND  
24                         THIS IS ACTUALLY WHERE WE HAVE PROVIDED MORE DETAIL.  
25                         AND IN THE NEXT SLIDES I'M GOING TO WALK THROUGH THE

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1 PDEV AND THE CLIN2 RUBRICS. IN BOTH CASES THE KEY  
2 THING TO KEEP IN MIND IS THAT THESE ARE ALIGNMENT  
3 AND QUALIFICATION TOOLS, AND THEY ARE NOT  
4 SUBSTITUTES FOR SCIENTIFIC REVIEW.

5 ARE WE ALL OKAY? GOOD.

6 SO THE PDEV PROGRAM IS INTENDED TO ENRICH  
7 CIRM'S CLINICAL PIPELINE. COMPARED TO THE EXISTING  
8 PORTFOLIO, IT SHOULD ADVANCE STATE-OF-THE-ART  
9 THERAPEUTIC TECHNOLOGIES THAT ADDRESS A BROAD RANGE  
10 OF DISEASES AFFECTING CALIFORNIANS.

11 THE FIRST LINE THAT WE HAVE IN THE  
12 PRESUBMISSION RUBRIC FOR PDEV REFLECTS ALIGNMENT  
13 WITH CORE AREAS WHERE CIRM HAS A CLEAR ROLE AND  
14 RESPONSIBILITY EITHER BECAUSE OF STATUTE OR BECAUSE  
15 OF DOWNSTREAM ACCESS AND FEASIBILITY CONSIDERATIONS.  
16 APPLICANTS RECEIVE UP TO THREE POINTS IF THEIR  
17 PROJECT ALIGNS WITH AT LEAST ONE OF THESE AREAS:  
18 PLURIPOTENT STEM CELL-DERIVED THERAPIES, DISEASES OF  
19 THE CENTRAL NERVOUS SYSTEM, OR IN VIVO GENE  
20 THERAPIES. IMPORTANTLY, THIS IS NOT ADDITIVE.  
21 MEETING ONE CRITERION IS ENOUGH TO GET THE THREE  
22 POINTS. AND THIS WAS DESIGNED DELIBERATELY TO AVOID  
23 STACKING MODALITY BIAS OR FORCING PROJECTS TO FIT  
24 MULTIPLE BOXES.

25 THE NEXT SET OF PREFERENCES CAPTURES

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1 READINESS AND TRANSLATIONAL MOMENTUM. THIS INCLUDES  
2 NONVIRAL NUCLEIC ACID DELIVERY, EVIDENCE OF EARLY  
3 FDA ENGAGEMENT THROUGH A PRE-IND OR INTERACT  
4 MEETING, AS WELL AS PROGRESSION FROM EARLIER CIRM  
5 PROGRAMS, SUCH AS DISC<sup>2</sup> OR TRAN<sup>1</sup>. THE SIGNALS HELP  
6 US UNDERSTAND WHERE A PROJECT SITS ON THE  
7 DEVELOPMENT PATH AND WHETHER CIRM FUNDING IS LIKELY  
8 TO BE CATALYTIC AT THIS STAGE. AGAIN, THESE ARE  
9 PREFERENCES AND NOT REQUIREMENTS.

10 THE NEXT ONE IS UNDERREPRESENTED DISEASE  
11 AREAS. THIS CATEGORY IS ABOUT PORTFOLIO BALANCE, AS  
12 I WAS MENTIONING, AND IT GOES WITH THE DIVERSITY  
13 GUIDING PRINCIPLE. WE EXPLICITLY LOOK AT HOW  
14 REPRESENTED DISEASE AREA ALREADY IS WITHIN CIRM'S  
15 ACTIVE AWARDS AND GIVES MODEST ADDITIONAL WEIGHT TO  
16 AREAS THAT ARE UNDERREPRESENTED. THE INTENT HERE IS  
17 DIVERSIFICATION, NOT PRIORITIZATION OF RARITY OR  
18 EXCLUSION OF WELL-REPRESENTED DISEASES.

19 VICE CHAIR BONNEVILLE: ROSA, THAT POINT  
20 SYSTEM IS VARIABLE, ZERO TO TWO. CAN YOU EXPLAIN  
21 THAT A LITTLE MORE?

22 DR. CANET-AVILES: YES. WE CAN EXPLAIN  
23 THAT A LITTLE MORE. BASICALLY YOU HAVE -- THE ZERO  
24 TO TWO POINTS, YOU GET ZERO IF THE DISEASE AREA IS  
25 MORE THAN 10 PERCENT. ONE IS THE DISEASE AREA IS

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1 BETWEEN 5 PERCENT AND LESS THAN 10 PERCENT. AND TWO  
2 POINTS IS THE DISEASE AREA IS 5 PERCENT OR LESS.  
3 AGAIN, ONE OF THE THINGS I WAS GOING TO MENTION IS  
4 THAT SOME OF THESE SCORING METHODS HAVE, THIS IN  
5 PARTICULAR, HAD A SLIGHT MODIFICATION BETWEEN THE  
6 FIRST AND THE SECOND ROUND THAT I CAN ASK SHYAM TO  
7 SPEAK ABOUT A LITTLE BIT MORE IF YOU WANT. GOOD?

8 VICE CHAIR BONNEVILLE: THAT'S FINE.

9 DR. CANET-AVILES: THANK YOU. WHERE WERE  
10 WE?

11 VICE CHAIR BONNEVILLE: NOVELTY.

12 DR. CANET-AVILES: NOVELTY CRITERIA.  
13 THANK YOU. THE NOVELTY CRITERIA EXISTS SPECIFICALLY  
14 TO PREVENT PREFERENCES FROM BECOMING EXCLUSIONARY  
15 AND TO ENSURE THAT STRONG OUTLIER IDEAS STILL HAVE A  
16 WAY TO MOVE FORWARD EVEN WHEN THEY DON'T SCORE  
17 POINTS ON MULTIPLE PREFERENCES.

18 NEXT ONE IS THE CLIN2 QUALIFICATION  
19 RUBRIC. THIS SLIDE SUMMARIZES THE CLIN2  
20 QUALIFICATION RUBRIC WHICH IS USED AS AN INTERNAL  
21 SCREENING TOOL BY THE REVIEW TEAM TO DETERMINE WHICH  
22 APPLICATIONS MOVE FORWARD TO ARS REVIEW. IT IS NOT  
23 A SCIENTIFIC SCORING RUBRIC, AND IT DOES NOT REPLACE  
24 PEER REVIEW. EACH ITEM HERE REFLECTS A DISCRETE  
25 PREFERENCE DESIGNED TO ASSESS ALIGNMENT WITH THE

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1 GUIDING PRINCIPLES I MENTIONED A COUPLE SLIDES AGO.

2 THE FIRST SET OF PREFERENCES INCLUDES  
3 PLURIPOTENT STEM CELL-DERIVED THERAPIES AND DISEASES  
4 OF THE CNS. EVERYTHING IS ALIGNED ALSO WITH PDEV  
5 WHICH ARE EXPLICIT PROP 14 PRIORITIES. IN VIVO GENE  
6 THERAPY IS INCLUDED HERE INDIRECTLY, RESPONDING TO  
7 STATUTORY MANDATE BECAUSE OF ITS POTENTIAL FOR  
8 SCALABLE DELIVERY AND BROADER PATIENT ACCESS. SO  
9 THE STATUTORY MANDATE COULD LINK TO ACCESSIBILITY.

10 NONVIRAL GENETIC THERAPIES ARE INCLUDED TO  
11 RECOGNIZE EMERGING APPROACHES THAT MAY REDUCE SAFETY  
12 OR MANUFACTURING CONSTRAINTS. WE ALSO ACCOUNT  
13 WITHIN THE CLIN2 QUALIFICATION RUBRIC FOR  
14 ACCELERATED REGULATORY DESIGNATION SUCH AS RMAT OR  
15 BREAKTHROUGH OR FAST TRACK BECAUSE MATERIALLY THEY  
16 CHANGE THE DEVELOPMENT TIMELINES AND SIGNAL  
17 REGULATORY ALIGNMENT. PROGRESSION FROM EARLIER CIRM  
18 AWARDS IS ALSO REFLECTING STEWARDSHIP OF PRIOR  
19 INVESTMENTS. AND CALIFORNIA-BASED ORGANIZATIONS  
20 REFLECT THE TAXPAYER-FUNDED NATURE OF THE PROGRAM.  
21 FINALLY, PIVOTAL TRIALS RECEIVE ADDITIONAL WEIGHT  
22 BECAUSE THEY REPRESENT THE FASTEST AND MOST DIRECT  
23 PATH TO POTENTIAL LICENSURE AND PATIENT IMPACT.

24 VICE CHAIR BONNEVILLE: ROSA, CAN YOU GO  
25 BACK TO THE PDEV QUALIFICATIONS REALLY QUICKLY?

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1 SO THE TARGET -- THE UNDERREPRESENTED IN  
2 CIRM ACTIVE PORTFOLIO THAT HAS A ZERO TO TWO, IS  
3 THAT NOT SOMETHING -- YOU SAID THAT ALL THE PDEV AND  
4 CLIN HAD THE SAME QUALIFICATIONS. THEY WERE JUST  
5 USED DIFFERENTLY. SO HERE IT IS, FOR THE  
6 PRESUBMISSION, THE LAST TWO, THE TARGETING DISEASE  
7 AREA AND THEN THE NOVELTY. SO WHERE DOES THAT COME  
8 INTO PLAY IN THE CLIN BECAUSE PART OF, I THINK,  
9 CONVERSATION HAS BEEN AROUND THE PREFERENCES WERE, I  
10 THINK WHAT THE BOARD -- THE DISCUSSION THE BOARD HAD  
11 WAS, LIKE YOU MENTIONED, WE DIDN'T WANT PREFERENCES  
12 TO BE LIMITING. AND SO I GUESS -- THOSE TWO WOULD  
13 SEEM TO HELP WITH THAT REQUEST. I DON'T SEE THEM  
14 LISTED IN THE CLIN, AND I DON'T KNOW THAT I NOTICED  
15 THAT BEFORE.

16 DR. CANET-AVILES: YEAH. GREAT QUESTION.  
17 SHOWS THAT YOU ARE PAYING A LITTLE ATTENTION.

18 VICE CHAIR BONNEVILLE: I DON'T KNOW ABOUT  
19 THAT.

20 DR. CANET-AVILES: YOU ARE LISTENING TO  
21 ME. YEAH. NO, THAT'S A VERY GOOD QUESTION, MARIA.

22 AND THE TWO CRITERIA THAT YOU ARE SPEAKING  
23 TO, WHICH ARE VERY IMPORTANT, AND THEY ALIGN VERY  
24 STRONGLY WITH THE SIXTH GUIDING PRINCIPLE WHERE IN  
25 THE QUALIFICATION RUBRIC OF THE POSTED CLIN2 PROGRAM

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1 ANNOUNCEMENT THEY GET TRANSLATED INTO THE  
2 QUALIFICATION SCORING PROCESS WHICH INCLUDES  
3 TIEBREAKING CRITERIA THAT WE HAVEN'T TALKED ABOUT.  
4 AND THE REVIEW TEAM DOES THIS. AND I'M GOING TO  
5 DEFER TO MY COLLEAGUE, DR. SAMBRANO, TO EXPLAIN HOW  
6 THIS WAS TRANSLATED.

7 VICE CHAIR BONNEVILLE: I'M JUST CURIOUS  
8 WHY HERE, WHY IS IT DONE AS A TIEBREAKER HERE, BUT  
9 IT'S USED DIFFERENTLY IN PDEV IF THAT'S WHAT WAS IN  
10 THE PROGRAM ANNOUNCEMENT OR THE CONCEPT PLAN --  
11 SORRY -- WHEN IT WAS DISCUSSED OR WAS IT NOT? I  
12 THOUGHT THAT'S WHAT WE WERE GETTING TO.

13 DR. SAMBRANO: OKAY. WELL, I'LL EXPLAIN  
14 HOW IT IS THAT IT'S DONE. I THINK PART OF IT IS  
15 THAT THESE WERE DEVELOPED SEPARATELY WITH THE  
16 DIFFERENT TEAMS. SO PDEV VERSUS CLIN. THE WAY CLIN  
17 WORKS IS THAT IT WAS FOLLOWING UP ON THE ESTABLISHED  
18 QUALIFICATION PROCESS THAT WE HAD IN PLACE ALREADY.  
19 AND SO THE CRITERIA AND HOW THAT WORKS IS WE START  
20 WITH OBJECTIVE CRITERIA THAT WE NEED TO ASSESS. AND  
21 SO THAT STEP IS DONE AND THE PREFERENCES ARE SUCH AS  
22 LISTED HERE THAT CAN BE ASCERTAINED VERY CLEARLY ONE  
23 WAY OR THE OTHER AND DONE QUICKLY. THAT WILL LEAD  
24 YOU TO A HIERARCHY OF THESE PROJECTS THAT THEN WE  
25 TIE-BREAK.

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1           AND SO THE FIRST STEP IN TIEBREAKING IS TO  
2 BRING IT TO THE GRANTS WORKING GROUP. AND SO THEY  
3 ASSESS THE VALUE PROPOSITION. AND SO WITH THAT  
4 VALUE PROPOSITION, THEY'RE LOOKING AT THREE  
5 QUESTIONS. THEY'RE LOOKING AT THE POTENTIAL TO  
6 PROVIDE MEANINGFUL AND SUBSTANTIAL IMPROVEMENT IN  
7 CLINICAL OUTCOMES, EXPECTED IMPACT OF ADDRESSING THE  
8 UNMET MEDICAL NEED ON PATIENTS, CAREGIVERS,  
9 HEALTHCARE SYSTEM. AND THEN THIRD, THE FEASIBILITY  
10 AND PRACTICALITY OF THE THERAPY UPTAKE BY PATIENTS,  
11 HEALTHCARE PROVIDERS, AND PAYERS. AND SO THEY SCORE  
12 AGAINST THAT IN ORDER TO BREAK TIES.

13           AND WHERE WE INSERTED THE NOVELTY, AT  
14 LEAST IN THE CURRENT PROCESS, IS SHOULD THERE STILL  
15 BE A TIE, THEN THE CLINICAL TEAM WOULD USE THAT IN  
16 ORDER TO DISTINGUISH BETWEEN APPLICATIONS THAT WOULD  
17 ADVANCE OR WOULD NOT.

18           BUT IN TERMS OF THINKING ABOUT  
19 PREFERENCES, I THINK ONE OF THE THINGS IS THESE ARE  
20 NOT MEANT, AND I THINK WE'VE SAID IT BEFORE, TO BE  
21 STATIC. OUR EXPECTATION IS THAT OVER TIME THESE ARE  
22 GOING TO CHANGE. AND DEPENDING ON WHAT WE GET, WE  
23 WANT TO CHANGE THEM SO THAT WE CAN --

24           VICE CHAIR BONNEVILLE: EVOLVE.

25           DR. SAMBRANO: YES, EVOLVE, TWEAK THEM,

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1 AND SO ON. SO I THINK EVEN THOUGH NOVELTY WE KIND  
2 OF PUSH TO THE BACK, AND PART OF THE REASON WAS THAT  
3 WE THOUGHT IT TO BE MORE SUBJECTIVE THAN THE OTHERS  
4 THAT WE HAD AND HARDER TO ASSESS AS SUCH, BUT I  
5 THINK THERE ARE WAYS IN WHICH YOU CAN MAKE NOVELTY  
6 MORE OBJECTIVE, WHICH IS KIND OF ALIGNED WITH WHAT  
7 PDEV IS DOING IN TERMS OF YOU DEFINE A SPECIFIC  
8 PORTFOLIO LIKE OUR CLIN PORTFOLIO. IT'S EITHER IN  
9 THERE OR IT'S NOT. IF IT'S NOT, THEN WE GIVE THE  
10 POINT. IF IT IS, WE DON'T OR HOWEVER. SO YOU CAN  
11 MAKE IT OBJECTIVE IF WE CHOOSE TO DO THAT GOING  
12 FORWARD, BUT, AGAIN, WITH THE EXPECTATION THAT WE  
13 WILL EVOLVE IT.

14 VICE CHAIR BONNEVILLE: THANK YOU.

15 DR. CANET-AVILES: THANK YOU, GIL. AND  
16 ONE WAY OF EVOLVING THIS, AND THIS CAN BE PART OF  
17 THE DISCUSSION IN MARCH, EVEN TODAY INCLUDING TO  
18 MARCH IS THAT WE COULD ADD THE NOVELTY CRITERIA AS  
19 PART OF ONE OF THE MAIN QUALIFICATION CRITERIA AS  
20 GIL IS SAYING. AND THAT COULD BE A RECOMMENDATION  
21 BASED ALSO ON THIS STRONG MESSAGE THAT WE ARE  
22 GETTING FROM SOME PRE-CALLS AND FROM BOARD MEMBERS  
23 AFTER WE POSTED THAT THE OUTLIERS GET MISSED. AND  
24 WE WANT TO ENSURE THAT STRONG OUTLIER IDEAS STILL  
25 HAVE A WAY TO MOVE FORWARD EVEN WHEN THEY DON'T

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1 SCORE POINTS ON MULTIPLE PREFERENCES.

2 WITH THAT SAID, I WAS NOTIFIED THAT WE HAD  
3 MADE A CHANGE, AND THIS IS IMPORTANT. IF YOU CAN GO  
4 TO THE PDEV, JUST FOR ANY APPLICANTS THAT ARE  
5 LISTENING, IT'S IMPORTANT. YOU SEE THE TARGETING  
6 DISEASE AND UNDERREPRESENTED AREA IS ACTUALLY ONE  
7 POINT, AND IT'S THE NOVELTY, THE ONE THAT HAS ZERO  
8 TO TWO POINTS. JUST WANT TO CLARIFY THIS, AND WE  
9 WILL UPDATE THIS FOR THE BOARD MEETING. IT WAS A  
10 MISTAKE WE MADE WHEN WE POSTED THIS SLIDE. OKAY?

11 MS. MANDAC: CHRIS HAD HER HAND RAISED.  
12 CHRIS, JUST DOUBLE-CHECKING.

13 DR. MIASKOWSKI: GIL ANSWERED MY QUESTION.  
14 I WAS WONDERING ABOUT THE PROCESS TO DO THIS  
15 EVALUATION. SO THANKS.

16 DR. CANET-AVILES: AND, AGAIN, THIS IS  
17 DIFFERENT FOR THE PDEV, THE PRESUBMISSION RUBRIC,  
18 BECAUSE THESE ARE PRESUBMISSIONS THAT IS EVALUATED  
19 IN A VERY OBJECTIVE WAY BY THE TEAM. THERE IS A  
20 WHOLE PROCESS. FOR THE QUALIFICATION IS ACTUALLY  
21 THE REVIEW TEAM TOGETHER WITH GRANTS WORKING GROUP  
22 FOR THOSE THAT ARE MORE SUBJECTIVE CRITERIA.

23 WITH THAT, WE'RE GOING INTO SLIDE NO. 16.  
24 THANK YOU, LIZ. WITH THAT FRAMEWORK, I KNOW I USE  
25 THAT WORD A LOT, WE'LL NOW SHOW RESULTS FROM THE

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1 FIRST TWO CYCLES OF PDEV AND CLIN2 TO ILLUSTRATE HOW  
2 THESE PREFERENCES PLAYED OUT IN PRACTICE STARTING  
3 WITH CYCLE 1.

4 JUST A CLARIFICATION, FOR CYCLE 1, WE HAVE  
5 AN ARS FOR BOTH PDEV AND CLIN2. FOR CYCLE 2, WE  
6 ONLY HAVE THE PRESUBMISSION AND THE QUALIFICATION  
7 CRITERIA. THOSE HAVE NOT BEEN -- WELL, WE DON'T  
8 HAVE THE RESULTS OF THE MEETING. OKAY.

9 THIS SLIDE WILL SUMMARIZE HOW THE  
10 PREFERENCE FRAMEWORK PLAYED OUT IN THE FIRST PDEV  
11 CYCLE. WE RECEIVED 168 PRESUBMISSIONS REFLECTING  
12 WHAT I WAS SAYING, A STRONG DEMAND AND STRONG  
13 SCIENCE MOST LIKELY. USING THE PRESUBMISSION  
14 RUBRIC, WE INVITED 33 APPLICATIONS FORWARD FOR FULL  
15 APPLICATION AND REVIEW, WHICH CORRESPONDS ROUGHLY TO  
16 THE TOP 20 PERCENT. AND WHAT'S IMPORTANT HERE IS  
17 THE SEPARATION SIGNAL. AMONGST THE INVITED GROUP,  
18 97 PERCENT MET THREE TO FOUR OF THE STATED  
19 PREFERENCES; WHEREAS, 42 PERCENT OF THE NONINVITED  
20 PROPOSALS MET ZERO OR NON-PREFERENCES. THIS TELLS  
21 US THAT THE RUBRIC WAS FUNCTIONING AT LEAST AS  
22 INTENDED, NOT EXCLUDING AREAS ARBITRARILY, BUT  
23 HELPING DISTINGUISH WHICH PROPOSALS WERE MOST  
24 ALIGNED WITH THE PRIORITIES THAT THE BOARD HAD SET  
25 WHEN APPROVING THE CONCEPTS.

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1 OF THE 12 ULTIMATELY FUNDED AWARDS, WE SEE  
2 SEVERAL CONSISTENT THEMES. THERE WAS A CLEAR  
3 INCREASE IN PROPOSALS WITH STRONGER TRANSLATIONAL  
4 READINESS, INNOVATION, AND SCALABILITY. AND MORE  
5 THAN HALF REPRESENT PROGRESSIONS OF PRIOR  
6 CIRM-FUNDED PROGRAMS. AND THE FUNDED SET IS MORE  
7 ENRICHED FOR DISEASE AREAS THAT HAD BEEN  
8 UNDERREPRESENTED IN OUR ACTIVE PORTFOLIO. TAKEN  
9 TOGETHER, THIS CYCLE RESULTS SUGGESTS THAT THE  
10 PREFERENCES ARE NOT NARROWING THE SCIENCE, BUT  
11 REBALANCING THE PRECLINICAL PORTFOLIO ACROSS  
12 MODALITY, DISEASE AREA, AND PROP 14 CNS PRIORITIES  
13 IN A WAY THAT IS INTENTIONAL AND ALIGNED WITH WHAT  
14 WE WERE SET TO DO BY THE BOARD WHEN THEY APPROVED  
15 OUR STRATEGY. NEXT SLIDE.

16 THIS SLIDE SHOWS THE DATA FROM THE SECOND  
17 CYCLE OF PDEV. AN IMPORTANT CAVEAT IS THAT THESE  
18 PRESUBMISSION RESULTS -- THESE ARE PRESUBMISSION  
19 RESULTS ONLY. WE HAVE NOT YET COMPLETED FULL  
20 APPLICATION REVIEW OR GRANTS WORKING GROUP  
21 ASSESSMENT. WHAT WE SEE, HOWEVER, IS THAT THE SAME  
22 PATTERN FROM CYCLE 1 HOLDS. WE RECEIVED 126  
23 PRESUBMISSIONS AND INVITED 23 TO FULL APPLICATION,  
24 WHICH IS ABOUT ROUGHLY 18 PERCENT. IMPORTANTLY, A  
25 HUNDRED PERCENT OF INVITED APPLICATIONS MET THREE TO

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1 FIVE PREFERENCES WHILE ABOUT A THIRD OF UNINVITED  
2 APPLICATIONS MET ZERO TO ONE PREFERENCE. SO THE  
3 SIGNAL REMAINS WITH THE CLIN.

4 TWO ADDITIONAL POINTS RESPOND DIRECTLY TO  
5 QUESTIONS THAT WE'VE HAD. FIRST, WE INVITED -- THE  
6 INVITED POOL SPANS BROAD DISEASE AREAS, INCLUDING  
7 MORE CANCER AND IMMUNOLOGY PROGRAMS THAN IN CYCLE 1.  
8 AND SECOND, NEARLY 40 PERCENT OF INVITED  
9 APPLICATIONS COULD REPRESENT PROGRESSION WITHIN THE  
10 CIRM -- EXISTING CIRM PORTFOLIO IF FUNDED, WHICH IS  
11 EXACTLY WHAT WE INTENDED, DISCIPLINED ADVANCEMENT,  
12 NOT RANDOM EXPANSION. SO WHILE FINAL FUNDING  
13 DECISIONS ARE STILL AHEAD, THE TAKEAWAY IS THAT THE  
14 PREFERENCE FRAMEWORK CONTINUES TO DO WHAT IT WAS  
15 DESIGNED TO DO, WHICH IS IDENTIFY THE STRONGEST,  
16 MOST ALIGNED PROGRAMS EARLY WHILE ALLOWING THE  
17 PORTFOLIO TO GROW ACROSS DISEASE AREAS WHERE THE  
18 SCIENCE IS READY.

19 NOW WE'RE GOING TO GO INTO THE CLIN2  
20 CYCLE. I DON'T KNOW IF THERE ARE ANY QUESTIONS, IF  
21 YOU WANTED ME TO STOP. I'M GOING TO KEEP GOING, BUT  
22 FEEL FREE TO STOP ME. OKAY.

23 I'LL NOW TURN TO CYCLE 1 OF CLIN2. WE  
24 RECEIVED 23 TOTAL APPLICATIONS ALL OF WHICH WERE  
25 RANKED USING THE PREFERENCE POINTS AS PART OF THE

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1 QUALIFICATION. FROM THOSE, SEVEN ADVANCED TO FULL  
2 REVIEW AND FOUR WERE ULTIMATELY FUNDED. A FEW  
3 THINGS ARE WORTH HIGHLIGHTING. FIRST, ALL SEVEN  
4 APPLICATIONS THAT ADVANCED TO FULL REVIEW MET THREE  
5 TO FOUR PREFERENCE POINTS. SO THE FRAMEWORK CLEARLY  
6 DISTINGUISHED TOP TIER. ALL SEVEN TARGETED CNS  
7 INDICATIONS, WHICH IS CONSISTENT WITH ONE OF PROP 14  
8 PRIORITIES, AND SIX OR SEVEN INVOLVED EITHER  
9 PLURIPOTENT STEM CELL-DERIVED THERAPIES OR IN VIVO  
10 GENETIC THERAPIES, AND FOUR ALREADY HAD ADVANCE  
11 REGULATORY DESIGNATIONS WHICH SPEAKS TO DEVELOPMENT  
12 MATURITY.

13 LOOKING AT THE FUNDED PROGRAMS, ALL FOUR  
14 THAT WE FUNDED HAVE PHYSICAL DELIVERY PATHS ALIGNED  
15 WITH OUR ACCESS AND AFFORDABILITY STRATEGY AND THREE  
16 REPRESENT PROGRESSIONS OF CIRM-FUNDED PROGRAMS. AND  
17 THAT TELLS US THAT THE SYSTEM IS REINFORCING BOTH  
18 INNOVATION AND DISCIPLINED PORTFOLIO ADVISEMENT.  
19 THE KEY TAKEAWAY IS THAT THE SYSTEM WORKED  
20 DIRECTIONALLY AS INTENDED. IT ELEVATED PROGRAMS  
21 THAT ARE ALIGNED WITH THE STATUTORY PRIORITIES,  
22 CLINICAL READINESS, AND DELIVERY FEASIBILITY. THAT  
23 SAID, CYCLE 1 ALSO MADE CLEAR THAT THE RELATIVE  
24 WEIGHING OF PREFERENCE MATTERS, AND THAT'S WHERE  
25 REFINEMENT COULD COME IN TO ENSURE WE ARE NOT

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1 OVERCONCENTRATING SIGNALS AS THE PORTFOLIO GROWS.

2 THE NEXT SLIDE IS THE SECOND CYCLE OF  
3 CLIN2. AND I'M GOING FASTER BECAUSE I JUST REALIZED  
4 THE TIME. AND SCOTT IS GOING TO KILL ME. THIS  
5 SLIDE SHOWS WHERE WE ARE FOR -- AND CLAUDETTE  
6 TOO -- CLIN2 CYCLE, RECOGNIZING THAT THESE ARE  
7 INTERIM RESULTS PENDING GRANTS WORKING GROUP REVIEW  
8 AND BOARD APPROVAL.

9 WE RECEIVED 21 APPLICATIONS ALL OF WHICH  
10 WERE RANKED USING THE SAME PREFERENCE-BASED  
11 FRAMEWORK. FROM THOSE, SEVEN ADVANCED TO FULL  
12 REVIEW, AND EVERY ADVANCING APPLICATION SCORED THREE  
13 TO FOUR PREFERENCE POINTS, WHICH IS CONSISTENT WITH  
14 WHAT WE SAW IN CYCLE 1. IN TERMS OF COMPOSITION,  
15 FOUR TARGET CNS, FIVE REPRESENT PROGRESSIONS FROM  
16 THE EXISTING CIRM PORTFOLIO, AND FIVE ARE EITHER IN  
17 VIVO GENETIC THERAPIES OR PLURIPOTENT STEM  
18 CELL-DERIVED THERAPIES, AGAIN, REFLECTING A STRONG  
19 ALIGNMENT WITH THE PREFERENCES THAT THE BOARD SET.

20 FINAL FUNDING RECOMMENDATIONS WILL FOLLOW  
21 THE REVIEW OF JANUARY 27 AND THEN COME BACK TO THE  
22 BOARD THROUGH THE NORMAL APPROVAL PROCESS.

23 SO NOW I'M GOING TO SUMMARIZE. WHEN WE  
24 LOOK ACROSS PDEV AND CLIN2 -- I'M ALREADY, YEAH.  
25 TOGETHER THE OVERALL PATTERN IS CONSISTENT AND

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1 DIRECTIONALLY ALIGNED WITH WHAT THE BOARD ASKED US  
2 TO DO. AWARDS IN BOTH PROGRAMS REFLECT THE  
3 INNOVATION, READINESS, ACCESS AND AFFORDABILITY, AND  
4 CNS CRITERIA THAT WERE EXPLICITLY LAID OUT IN THE  
5 PROGRAM ANNOUNCEMENTS, NOT INFORMALLY, BUT  
6 OPERATIONALLY THROUGH THE QUALIFICATION AND RANKING  
7 PROCESS.

8 THE APPLICATIONS THAT ADVANCED WERE  
9 LARGELY CIRM PORTFOLIO PROGRESSIONS. AND WE'VE HAD  
10 A LOT OF QUESTIONS ABOUT THAT, AND I JUST WANT TO  
11 MAKE THAT POINT. BUT IMPORTANTLY, THEY WERE NOT  
12 ADVANCING BECAUSE THEY WERE LEGACY PROJECTS. THEY  
13 ADVANCED BECAUSE THEY ALSO MET OTHER MULTIPLE STATED  
14 PREFERENCES. SO MANY OF THEM HAD SEVERAL  
15 PREFERENCES THAT THEY WERE HITTING.

16 ANOTHER RESULT, THE PORTFOLIO NOW INCLUDES  
17 MORE FEASIBLE AND SCALABLE MODALITIES WHICH  
18 STRENGTHENS DOWNSTREAM ACCESS AND AFFORDABILITY  
19 POTENTIAL WITHOUT SACRIFICING SCIENTIFIC RIGOR.  
20 THAT SAID, I WANT TO BE CLEAR ABOUT THE CAVEATS.  
21 THESE ARE EARLY SIGNALS, AND IT IS TOO SOON TO  
22 ASSESS PORTFOLIO LEVEL IMPACT. WHAT WE CAN SAY AT  
23 THIS STAGE IS THAT THE SYSTEM IS BEHAVING  
24 DIRECTIONALLY AS WE INTENDED.

25 NEXT I'M GOING TO GO INTO THE DISC4. THIS

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1 IS A BRIEF REMINDER OF WHAT THE BOARD APPROVED LAST  
2 YEAR FOR DISC4. THE BOARD APPROVED NEUROLOGICAL  
3 DISEASE AS A PREFERENCE FOR THE FY 25/26 DISC4  
4 CYCLE. AND THE PROGRAM WAS OPEN TO ALL COMERS. AS  
5 A REMINDER, THIS SLIDE SHOWS HOW THAT ALTERNATIVE  
6 STRUCTURE IS INTENDED TO WORK OVER TIME. SOME  
7 CYCLES ARE DRIVEN BY THE NEURO TASK FORCE IDENTIFIED  
8 NEEDS, WHICH WOULD BE THE ONES THAT ARE NTF BASED,  
9 RIGHT, AND WE JUST HAD ONE. AND WE HAD THE  
10 NEUROPSYCHIATRIC/NEURODEVELOPMENTAL PRIORITIES AND  
11 THEN WE HAD THE NEUROLOGICAL FOCUS. ALL THIS  
12 REFLECTS BOARD-SET PREFERENCES, AND CRUCIALLY EVERY  
13 CYCLE REMAINS OPEN TO ALL COMERS.

14 THIS STRUCTURE WILL GIVE THE BOARD A  
15 REPEATABLE, TRANSPARENT WAY TO SET DIRECTION YEAR  
16 OVER YEAR WHILE WE STILL PRESERVE SCIENTIFIC BREADTH  
17 AND FLEXIBILITY. SO FOR THIS YEAR, WHEN WE SET THE  
18 NEUROLOGICAL, THIS SLIDE SHOWS HOW THE PREFERENCES  
19 WERE OPERATIONALIZED IN THE DISC4 25/26 CYCLE  
20 CONSISTENT WITH WHAT'S APPROVED IN THE PROGRAM  
21 ANNOUNCEMENT.

22 AND I WILL JUST SAY THAT THE SCORING WAS  
23 NOT PUBLISHED FOR ANY OF THESE PROGRAMS, AND THAT IS  
24 NOT IDEAL. THE REASON THAT HAPPENS WAS BECAUSE WE  
25 MOVED FAST TO HONOR OUR COMMITMENT TO LAUNCH THESE

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1 PROGRAMS QUICKLY. AND THE SCORING WAS FINALIZED  
2 DURING IMPLEMENTATION RATHER THAN BEFORE POSTING,  
3 WHICH WE SHOULD HAVE PUBLISHED AND WE WILL MOVING  
4 FORWARD.

5 SO WHAT WE ARE TRYING TO DO IS SHOW NOW  
6 HOW WE SCORE THESE THINGS SO EVERYBODY IS -- TO HAVE  
7 TRANSPARENCY. THE NEUROLOGICAL DISEASE, SO FOR  
8 DISC4, THE NEUROLOGICAL DISEASE PREFERENCE CARRIED  
9 36 PERCENT OF THE TOTAL SCORING WEIGHT. THAT WAS  
10 INTENTIONAL AND TRANSPARENT BECAUSE IT REFLECTS THE  
11 BOARD'S DECISION TO CLEARLY SIGNAL A PRIORITY FOR  
12 THIS CYCLE WHILE STILL KEEPING THE PROGRAM OPEN TO  
13 ALL APPLICANTS. YOU COULD COME NOT HAVING  
14 NEUROLOGICAL AND KEEPING EVERYTHING ELSE AND YOU  
15 MIGHT MAKE IT, RIGHT, BUT IT WILL BE HARD.  
16 IMPORTANTLY, PREFERENCE ALIGNMENT WAS NOT THE SOLE  
17 DRIVER OF RANKING. 64 PERCENT OF THE SCORE CAME  
18 FROM SCIENTIFIC SUBSTANCE WHICH WAS REPRESENTED BY  
19 RELEVANCE TO HUMAN DISEASE BIOLOGY,  
20 CROSS-DISCIPLINARY, AND SYSTEM LEVEL APPROACHES AS  
21 WELL AS INNOVATION IN STEM CELL OR GENETIC RESEARCH.  
22 IN OTHER WORDS, PROJECTS STILL HAD TO BE STRONG  
23 SCIENCE FIRST. THIS STRUCTURE IS DOING WHAT IT WAS  
24 DESIGNED TO DO, WHICH IS TRANSLATE BOARD LEVEL  
25 PRIORITIES INTO MEASURABLE SIGNAL WITHOUT COLLAPSING

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1 DISC4 INTO A SINGLE DISEASE PROGRAM OR EXCLUDING  
2 HIGH QUALITY WORK OUTSIDE THE PREFERENCE AREA.

3 I'M GOING TO GO INTO THE RESULTS. THIS  
4 SLIDE SHOWS HOW THE DISC4 NEURO PREFERENCE PLAYED  
5 OUT AT THE PRESUBMISSION STAGE. AND JUST AS A  
6 REMINDER, WE HAVE -- THIS HAS NOT BEEN REVIEWED.  
7 IT'S COMING IN FEBRUARY, THE REVIEW, FOR THIS  
8 PROGRAM.

9 WE RECEIVED 138 PRESUBMISSIONS AND 86  
10 PERCENT ALIGNED WITH THE NEURO PREFERENCE. THAT  
11 TELLS US THAT THE SIGNAL WAS CLEARLY HEARD BY THE  
12 COMMUNITY. FROM THAT POOL, 24 APPLICATIONS WERE  
13 INVITED TO FULL APPLICATION AND REVIEW. AND  
14 IMPORTANTLY, A HUNDRED OF THOSE INVITED MET THE  
15 NEURO PREFERENCE, BUT THEY SPAN A BROAD RANGE OF  
16 NEUROLOGICAL DISEASES AND REPRESENT A WIDE DIVERSITY  
17 OF MECHANISMS AND SCIENTIFIC APPROACHES.

18 SO WHAT WE ARE SEEING HERE IS NOT  
19 CONVERSION ON A SINGLE DISEASE OR MODALITY. IT'S  
20 ACTUALLY ENRICHMENT WITHIN A PRIORITY AREA WHILE  
21 PRESERVING SCIENTIFIC BREADTH. FUNDING DECISIONS  
22 ARE STILL PENDING, AS I MENTIONED, AND IT WILL BE IN  
23 FEBRUARY 2026, BUT AT THIS STAGE THE PREFERENCE IS  
24 DOING EXACTLY WHAT IT WAS DESIGNED TO DO, WHICH IS  
25 TO SHAPE THE POOL WITHOUT NARROWING THE SCIENCE.

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1           AND NOW I'M GOING TO MOVE INTO WHAT WE'VE  
2           LEARNED SO FAR. STEPPING BACK, THERE ARE -- THE  
3           INITIAL SIGNALS WE ARE SEEING FROM PREFERENCE  
4           SETTING ACROSS PDEV AND CLIN2. FIRST, THE  
5           APPLICATIONS THAT ADVANCED TO GRANTS WORKING GROUP  
6           REVIEW CONSISTENTLY MET MULTIPLE PREFERENCES. THAT  
7           TELLS US THAT THE RUBRIC IS DOING REAL TRIAGE. IT'S  
8           NOT ADVANCING PROJECTS ON A SINGLE ATTRIBUTE ALONE.

9           SECOND, IN CLIN2 WE SEE HIGH PROPORTION OF  
10          CNS-FUNDED PROJECTS, WHICH IS CONSISTENT WITH THE  
11          STATED PREFERENCE AND CONFIRMS THAT, WHEN WE WEIGH A  
12          PRIORITY, IT SHOWS UP CLEARLY AT THE OUTCOME LEVEL.  
13          IN CONTRAST, PDEV SHOWS A MUCH WIDER SPREAD ACROSS  
14          DISEASE AREAS AND MODALITIES, WHICH REFLECTS BOTH  
15          THE EARLY STAGE OF THE SCIENCE AND THE WAY  
16          PREFERENCES WERE DESIGNED TO GUIDE AND NOT CONSTRAIN  
17          THAT PORTFOLIO.

18          AND FINALLY, ACROSS BOTH PROGRAMS A LARGE  
19          FRACTION OF FUNDED PROJECTS ARE CIRM PORTFOLIO  
20          PROGRESSIONS, OVER 50 PERCENT IN PDEV AND ROUGHLY 75  
21          PERCENT IN CLIN2, WHICH SUGGESTS THAT THE SYSTEM IS  
22          REINFORCING CONTINUITY WHILE STILL APPLYING  
23          DIRECTIONAL FILTERS. IMPORTANTLY, THESE ARE EARLY  
24          SIGNALS AS, AGAIN, NO FINAL CONCLUSIONS. THE  
25          JANUARY PRESENTATION, AS I MENTIONED AT THE

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1 BEGINNING, IS MEANT TO TEE UP THE QUESTIONS FOR THE  
2 BOARD. AND IN MARCH WE'LL COME BACK WITH A FULL  
3 PORTFOLIO LEVEL ANALYSIS AND ANY PROPOSED  
4 REFINEMENTS BASED ON YOUR GUIDANCE.

5 MR. TOCHER: PAT HAS HIS HAND RAISED.

6 DR. CANET-AVILES: YES. I WAS JUST GOING  
7 TO PUT THE LAST SLIDE, BUT I'M HAPPY TO ANSWER  
8 QUESTIONS. I'LL JUST PUT THIS HERE. BASICALLY THIS  
9 SLIDE IS PLANNED ANALYSIS, AND PAT LEVITT, DR.  
10 LEVITT, ACTUALLY WAS THE ONE THAT BROUGHT THESE  
11 SUGGESTIONS. AND OUR QUESTION COULD BE BASED ON ALL  
12 WHAT WE SAW TODAY, WHAT OTHER ANALYSIS, IF ANY,  
13 WOULD WE LIKE TO SEE IN MARCH. AND WITH THAT, I  
14 THANK YOU FOR YOUR ATTENTION, AND I'M SORRY I WAS SO  
15 LONG. I DON'T KNOW IF I WAS LONG, BUT TRIED MY  
16 BEST. PAT.

17 DR. LEVITT: I JUST NEED A -- MAYBE TWO  
18 CLARIFICATIONS. ONE IS YOU HAD THAT SLIDE UP WHERE  
19 WE HAD THE INITIAL DISC WAS FOCUSED ON  
20 NEURODEVELOPMENTAL DISORDERS AND PSYCHIATRIC, AND  
21 THEN THIS ONE IS FOCUSED ON NEUROLOGICAL. RIGHT? I  
22 THINK THAT'S WHAT YOU SAID. AND I'M TRYING TO  
23 UNDERSTAND WHERE THIS FOCUS -- YOU SAID A HUNDRED  
24 PERCENT ARE NEURO, NEUROLOGICAL, BUT EXCLUDED  
25 NEURODEVELOPMENTAL AND PSYCHIATRIC, OR YOU MEANT

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1 NEURO MEANING THE NEURO DEFINED IN PROPOSITION 14,  
2 WHICH WAS ANY NERVOUS SYSTEM DISORDER.

3 DR. CANET-AVILES: THE NEURO DEFINED IN  
4 PROPOSITION 14, EVERYTHING. THAT WAS ACTUALLY WHAT  
5 YOU, THE BOARD, ASKED US TO HAVE THERE.

6 DR. LEVITT: RIGHT. I JUST THINK IT'S A  
7 LITTLE CONFUSING BECAUSE THERE ARE THINGS THAT ARE  
8 NEUROLOGICAL AND NOT, BUT THERE ARE THINGS THAT ARE  
9 NEURODEVELOPMENTAL THAT ARE NEUROLOGICAL. AND, OF  
10 COURSE, FOR SOME NEUROPSYCHIATRIC, IT'S ALSO  
11 NEUROLOGICAL. SO I DON'T KNOW -- TO ME THE  
12 TERMINOLOGY IS TO FOLLOW WHAT'S IN PROPOSITION 14  
13 BECAUSE THAT'S THE EMPHASIS AREA AND THAT'S HOW THE  
14 SCORING IS BEING DONE. IS IT NEURO BASED ON THE  
15 DEFINITION IN PROPOSITION 14?

16 DR. CANET-AVILES: YEAH. SO YOU HAVE A  
17 GREAT POINT, PAT. AND WE WILL CHANGE THAT TO MAKE  
18 SURE THAT IT ALIGNS WITH WHAT WE'VE DONE AND WHAT  
19 THE BOARD. SO WE WILL SAY NEURO AS DEFINED BY PROP  
20 14 INSTEAD OF NEUROLOGICAL, WHICH IS -- YEAH.

21 DR. LEVITT: AND THEN JUST THE OTHER  
22 CLARIFICATION I HAVE. SO THERE'S A POINT GIVEN IF  
23 IT'S NONVIRAL DELIVERY. AND ALTERNATIVE DELIVERIES  
24 FOR THE CENTRAL NERVOUS SYSTEM ARE FAR BEHIND OTHER  
25 ORGAN SYSTEMS. SO I'M WONDERING HOW THAT -- MAYBE

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1 IT'S TOO LONG A CONVERSATION TO HAVE, BUT I'M  
2 WONDERING HOW THAT PLAYED OUT BECAUSE, RIGHT,  
3 DELIVERY TO THE CNS, THERE'S BEEN MORE WORK DONE ON  
4 VIRAL DELIVERY THAN THERE HAVE BEEN ON ANYTHING  
5 ELSE, AND IT'S STILL BEHIND THE EIGHT BALL IN TERMS  
6 OF GETTING THESE OTHER -- LIPOSOMES AND OTHER THINGS  
7 ARE ACTUALLY TARGETING, NOT JUST INTO THE NERVOUS  
8 SYSTEM, BUT TARGETING THE RIGHT CELLS.

9 SO I'M WONDERING IF THAT ENDS UP BEING A  
10 DISADVANTAGE FOR SCORING.

11 AND THEN THE OTHER THING I'LL MENTION, AND  
12 WE DON'T HAVE TO DEAL WITH IT TODAY, MAYBE WE'LL  
13 DEAL WITH IT AT THE BOARD, IS THAT I GO BACK AND  
14 FORTH ON THIS ISSUE ABOUT UNDERREPRESENTED AREAS AND  
15 SO THAT GETS A PRIORITY. BECAUSE WE HAVE THIS  
16 LIMITED PERIOD OF TIME. THAT'S HOW MANY OF US ARE  
17 OPERATING. RIGHT? WHO KNOWS WHAT'S GOING TO HAPPEN  
18 AFTER THIS PERIOD OF TIME? ONE CAN MAKE THE  
19 ARGUMENT THAT AN AREA IN WHICH THERE'S BEEN A LOT OF  
20 ACTIVITY IS MAKING ADVANCES TO THE POINT WHERE,  
21 LIKE, THE NEXT PROJECT IS GOING TO BE THE  
22 BREAKTHROUGH PROJECT AS OPPOSED TO SOMETHING THAT IS  
23 WAY UNDERREPRESENTED, MEANING IT'S PROBABLY WAY  
24 BEHIND, NOT A LOT OF WORK HAS BEEN DONE ON IT, AND  
25 THAT'S GOING TO HAVE A LONGER TRAJECTORY TO GET TO

1 THE POINT.

2 SO I JUST RAISE THIS AS A POINT TO THINK  
3 ABOUT. AND I DO GO BACK AND FORTH BECAUSE, OF  
4 COURSE, WE WANT TO SEE A BROAD PORTFOLIO. BUT,  
5 ROSA, AS YOU DESCRIBED, THERE IS A BROAD PORTFOLIO.  
6 BUT SOMETIMES SOMETHING THAT'S BEEN WORKED ON A LOT  
7 IS AT THE POINT OF ANOTHER BREAKTHROUGH WHICH MOVES  
8 IT TO LIKE ANOTHER LEVEL BECAUSE THERE'S BEEN SO  
9 MUCH WORK ON IT AND SHOULDN'T BE -- MAYBE SHOULDN'T  
10 BE PENALIZED BECAUSE THERE'S BEEN A LOT OF WORK DONE  
11 ON IT AND CIRM HAS FUNDED THAT. SO MAYBE IT'S FOOD  
12 FOR THOUGHT, BUT WE DO WANT BREAKTHROUGHS AND WE DO  
13 HAVE A TIMELINE, AND FOR SOMETHING STARTING FROM  
14 SCRATCH MAY NOT BE OPTIMAL. I'LL STOP THERE.

15 DR. CANET-AVILES: OKAY. I THINK WE CAN  
16 DEFINITELY TALK ABOUT THIS IN MARCH. I THINK IT'S A  
17 VERY GOOD POINT THAT YOU ARE RAISING. AND I THINK  
18 THE WHOLE POINT ABOUT THE DELIVERY, I THINK THAT  
19 THERE ARE MULTIPLE DELIVERY SYSTEMS TO THE CNS THAT  
20 WORK AND SEVERAL ARE ALREADY IN THE CLINIC. AND WE  
21 CONTINUE TO FUND AND SUPPORT THIS. BUT A NONVIRAL  
22 DELIVERY, WE PRIORITIZED IT AS A STRATEGIC  
23 PREFERENCE BECAUSE IT HAS THE POTENTIAL TO OVERCOME  
24 CONSTRAINTS THAT VIRAL SYSTEMS STILL FACE, LIKE  
25 REDOSING LIMITATIONS AND MANUFACTURING SCALABILITY

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1 AND SUCH.

2 SO BASICALLY IT'S ABOUT PORTFOLIO BALANCE  
3 AND FUTURE OPTIONALITY, I COULD SAY, IN THIS CASE,  
4 BUT HAPPY TO DISCUSS FURTHER IN MARCH IF YOU WANT.

5 VICE CHAIR BONNEVILLE: I THINK WE SHOULD.

6 DR. CANET-AVILES: YEAH.

7 CHAIRMAN FISCHER-COLBRIE: I THINK THERE'S  
8 SOME OTHER QUESTIONS, RIGHT? WE CAN PROCEED.

9 DR. YVONNE CHEN: IS PUBLIC PARTICIPANT  
10 ALLOWED TO ASK A QUESTION RIGHT NOW?

11 MR. TOCHER: JUST A MINUTE. WE'RE FIRST  
12 GOING TO ENTERTAIN QUESTIONS FROM THE BOARD.

13 CHAIRMAN FISCHER-COLBRIE: ANY OTHER  
14 QUESTIONS FROM THE BOARD OR THE SCIENCE  
15 SUBCOMMITTEE?

16 MS. MANDAC: SO FOR MEMBERS OF THE PUBLIC,  
17 THE FLOOR IS OPEN AND WE'LL CALL ON YOU ONE BY ONE.  
18 YOU WILL SEE A TIMER ON THE TOP RIGHT-HAND CORNER OF  
19 YOUR ZOOM WINDOW. YOU WILL EACH HAVE THREE MINUTES.  
20 WE'LL START WITH DR. CHEN AND THEN MOVE ON TO  
21 DR. LIU-MICHAEL. DR. CHEN, THE FLOOR IS YOURS.

22 DR. YVONNE CHEN: GREAT. THANK YOU VERY  
23 MUCH. GOOD AFTERNOON. MY NAME IS YVONNE CHEN. I'M  
24 A PROFESSOR OF IMMUNOLOGY AT UCLA. I'D LIKE TO  
25 THANK THE SUBCOMMITTEE FOR YOUR TIME AS WELL AS THE

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1 CIRM STAFF FOR ALL OF YOUR EFFORT IN EXECUTING THE  
2 MISSIONS FOR CIRM.

3 I'M SPEAKING TODAY TO BRING TO YOUR  
4 ATTENTION AN IMPORTANT CONSEQUENCE OF THE PREFERENCE  
5 SYSTEM THAT DR. ROSA DISCUSSED WITH US IN DETAIL  
6 JUST NOW. AND SPECIFICALLY, IT'S A CONSEQUENCE THAT  
7 MAY OR MAY NOT HAVE BEEN INTENDED, AND IT WAS  
8 DESCRIBED AS PERCEPTION OF MODALITY BIAS IN DR.  
9 ROSA'S PRESENTATION. I'D LIKE TO DISCUSS WHY THIS  
10 IS NOT SIMPLY A PERCEPTION, BUT A REALITY.

11 BY VIRTUE OF LISTING SPECIFIC PREFERENCES  
12 IN TRIAGING APPLICATIONS BASED ON HOW MANY BOXES ONE  
13 COULD CHECK, THE PREFERENCE SYSTEM EFFECTIVELY  
14 ELIMINATES CERTAIN TREATMENT MODALITIES FROM  
15 CONSIDERATION. FOR EXAMPLE, FOR AN EX VIVO VIRALLY  
16 TRANSFUSED CAR-T CELL THERAPY, THE SAME KIND OF  
17 THERAPY THAT HAS BEEN APPROVED BY THE FDA AND HAS  
18 ACTUALLY TRANSFORMED TREATMENT FOR CANCER, SUCH AS  
19 B-CELL LYMPHOMA AND MULTIPLE MYELOMA, THERE ARE  
20 THREE BOXES THAT CAN NEVER BE CHECKED. THESE ARE IN  
21 VIVO, NONVIRAL, AND PLURIPOTENT STEM CELLS.

22 SO TO SIMPLIFY THE DISCUSSION, LET ME  
23 FOCUS JUST ON PDEV, BUT CLIN2 HAS THE SAME ISSUES.  
24 THERE'S A TOTAL OF SIX PREFERENCE BOXES IN PDEV. SO  
25 NOT BEING ABLE TO CHECK THREE OF THOSE BOXES MEANS

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1 CAR-T CELL THERAPY APPLICATIONS ARE IMMEDIATELY PUT  
2 AT A DISADVANTAGE THAT CAN NEVER BE OVERCOME  
3 REGARDLESS OF HOW STRONG THE SCIENCE IS.

4 AND IF THE THERAPY IS INTENDED FOR  
5 SOMETHING THAT'S NOT A CNS DISEASE, EVEN IF IT'S A  
6 HUGE UNMET MEDICAL NEED, SUCH AS LUNG CANCER,  
7 PANCREATIC CANCER, THAT'S ANOTHER BOX THAT WILL  
8 NEVER BE CHECKED. AND, THEREFORE, A PDEV  
9 APPLICATION FOR A CAR-T CELL THERAPY FOR LUNG  
10 CANCER, FOR EXAMPLE, WILL NEVER BE ABLE TO CHECK  
11 FOUR OUT OF SIX BOXES. SO THE MAXIMUM SCORE THAT  
12 CAN EVER BE ACHIEVED IS TWO, AND THAT DOOMS THE  
13 APPLICATION. IT WILL NEVER BE REVIEWED.

14 AND SO, AGAIN, WE'RE NOT EVEN CONSIDERING  
15 THE SCIENTIFIC MERIT. THIS IS SIMPLE BOX-CHECKING  
16 ARITHMETIC. AND IF WE LOOK AT THE LIST OF PDEV AND  
17 CLIN2 APPLICATIONS THAT WERE ACTUALLY FUNDED IN THE  
18 FIRST ROUND, THERE IS A COMPLETE ABSENCE OF CAR-T  
19 CELL THERAPIES. AND THIS IS WHY I SAY THIS IS NOT  
20 JUST A PERCEPTION. IT'S A REALITY OF THE PREFERENCE  
21 SYSTEM.

22 I SHOULD ALSO NOTE THAT, BASED ON THE  
23 TABLE THAT ROSA SHOWED ON SLIDE 11 OF HER DECK,  
24 WHICH IS A LITTLE DIFFERENT THAN THE TABLE THAT'S  
25 SHOWN IN THE RFA, ALL EX VIVO CAR-T CELL THERAPIES

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1 THAT'S NOT FOR CNS DISEASES WILL AUTOMATICALLY BE  
2 ELIMINATED BECAUSE THE FIRST LINE IS AT LEAST ONE OF  
3 THE FOLLOWING. AND NONE OF THOSE THREE THINGS COULD  
4 BE CHECKED.

5 NOW, I UNDERSTAND RESOURCES ARE LIMITED,  
6 AND IT IS THE CIRM BOARD'S DISCRETION TO DECIDE, BUT  
7 I WANT TO POINT THIS OUT --

8 MS. MANDAC: DR. CHEN, YOUR TIME IS UP.  
9 NEXT WE HAVE DR. LIU-MICHAEL AND THEN DR. CHEN.  
10 DR. LIU-MICHAEL, THE FLOOR IS YOURS.

11 DR. LIU-MICHAEL: HI. THANK YOU SO MUCH,  
12 ROSA, FOR THE PRESENTATION AND ESPECIALLY FOR THE  
13 CLARIFICATION OF THE PREFERENCES. I'M QING  
14 LIU-MICHAEL FROM CITY OF HOPE. SO I SHARE THE SAME  
15 OPINION AS DR. PAT LEVITT, JUST TO CLARIFY ABOUT THE  
16 CIRM PREFERENCES UNDERREPRESENTED AREAS. IF YOU CAN  
17 IN THE FUTURE OR NOW CLARIFY THAT, THAT WOULD BE  
18 GREAT.

19 SO -- BECAUSE WE'VE BEEN, SIMILAR TO DR.  
20 YVONNE CHEN, CITY OF HOPE HAS BEEN SUBMITTING A LOT  
21 OF CANCER-RELATED PROPOSALS AND HAVE ALSO KNOWN  
22 APPLICANTS TO HAVE SUBMITTED CNS-RELATED DISEASE  
23 THAT GOT TURNED AWAY BECAUSE OF CIRM  
24 UNDERREPRESENTED AREAS. SO, YEAH, ANY MORE  
25 CLARIFICATION ON THAT, THAT WILL BE GREAT.

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1 AND FINALLY, IF YOU CAN SHARE YOUR DECK  
2 SINCE IT'S DIFFERENT FROM THE ONE THAT'S SHARED ON  
3 THE WEBSITE, THAT WOULD BE GREAT. THANK YOU SO MUCH  
4 FOR THE PRESENTATION, AND THANK YOU ALL SO MUCH FOR  
5 YOUR WORK. THAT'S ALL.

6 MS. MANDAC: THANK YOU, DR. LIU-MICHAEL.  
7 DR. CHEN, THE FLOOR IS YOURS.

8 DR. JIA CHEN: HI, MEMBERS OF THE BOARD  
9 AND MEETING ATTENDEES. MY NAME IS JIA CHEN. I'M A  
10 CALIFORNIA RESIDENT AND PROFESSIONALLY AN  
11 ADMINISTRATOR FOR A RESEARCH CENTER AT THE  
12 UNIVERSITY OF CALIFORNIA, LOS ANGELES, AND SUPPORT  
13 PHYSICIAN/SCIENTISTS WHO TREAT CANCER PATIENTS USING  
14 CELL/GENE THERAPIES. MY PROFESSIONAL ROLE PROVIDES  
15 ME WITH AN OPPORTUNITY TO SUPPORT CANCER PATIENTS  
16 ACROSS CALIFORNIA WHO HAVE GREATLY BENEFITED FROM  
17 CELL AND GENE THERAPIES.

18 IN THAT REGARD, I WANT TO FIRST THANK THE  
19 ENTIRE CIRM TEAM AND ICOC BOARD MEMBERS WHO WORK  
20 TIRELESSLY TO MAKE ALL THIS POSSIBLE. IN DOING MY  
21 JOB, I HAVE SEEN HOW IMPACTFUL CIRM HAS BEEN IN THE  
22 FIELD OF CELL AND GENE THERAPY. BUT I DO HAVE THREE  
23 OBSERVATIONS TO BRING TO THE ATTENTION OF THE ICOC  
24 SCIENCE SUBCOMMITTEE REGARDING THE IMPLEMENTATION OF  
25 THE CIRM STRATEGIC ALLOCATION FRAMEWORK THUS FAR.

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1 THE FIRST IS THAT THE NEW PREFERENCE  
2 SELECTION PROCESS INTENTIONALLY OR UNINTENTIONALLY  
3 ALGORITHMICALLY EXCLUDES MANY CELL AND GENE THERAPY  
4 APPROACHES THAT HAVE DEMONSTRATED TO BE SAFE AND  
5 CLINICALLY EFFICACIOUS FOR PATIENTS. MANY OF THESE  
6 PHYSICIAN/SCIENTISTS LEADING SUCCESSFUL CELL THERAPY  
7 TRIALS ARE COMPLETING THEIR MULTIYEAR EFFORTS TO  
8 TRANSLATE CELL THERAPIES INTO FDA IND APPLICATIONS  
9 ARE SUDDENLY NOT HAVING THEIR CIRM APPLICATIONS  
10 REVIEWED SCIENTIFICALLY SINCE IMPLEMENTATION OF THE  
11 STRATEGIC ALLOCATION FRAMEWORK.

12 THE SECOND IS TO POINT OUT A PRACTICAL  
13 FACT, THAT CIRM-FUNDED CELL AND GENE RESEARCH  
14 PROGRAMS WHICH MIGHT BE MEETING MILESTONES AND  
15 SHOWING SUCCESS HAVE VERY LITTLE, IF ANY, FUNDING  
16 ALTERNATIVE TO CONTINUE ON THE PATH TOWARDS CLINICAL  
17 TRIAL OUTSIDE OF CIRM. THIS IS PARTICULARLY  
18 POIGNANT IN THE CURRENT RESEARCH FUNDING ENVIRONMENT  
19 IN OUR COUNTRY THAT IS DRASTICALLY DIFFERENT  
20 COMPARED TO WHEN THE STRATEGIC ALLOCATION FRAMEWORK  
21 WAS BEING DEVELOPED AND OPTIMIZED BY CIRM ABOUT TWO  
22 YEARS AGO.

23 MY LAST COMMENT IS THAT AS A CALIFORNIA  
24 TAXPAYER, I HAVE CONCERNS FOR A CIRM FUNDING  
25 PREFERENCE LIST THAT SKEWS THE FLOW OF STATE FUNDS

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1 TO PRIVATE COMPANIES INSTEAD OF AN APPLICATION  
2 SELECTION PROCESS THAT IS SOLELY BASED ON SCIENTIFIC  
3 MERIT. I THINK IT'S BECAUSE TWO OF THE EIGHT  
4 CRITERIA FOR CLIN2, BEFORE AN APPLICATION WILL BE  
5 SUBMITTED FOR SCIENTIFIC REVIEW, ARE AN ACCELERATED  
6 FDA DESIGNATION OR A PIVOTAL TRIAL, WHICH WOULD  
7 REQUIRE OR NEED ANTICIPATION OF A COMMERCIAL ENTITY  
8 TO APPLY AT THE FDA. TWO OUT OF EIGHT CRITERIA IS A  
9 STRONG SKEWING SELECTION FOR THE CIRM AWARD TOWARDS  
10 PRIVATE COMPANIES.

11 I THANK YOU FOR ALL YOUR ATTENTION.

12 MS. MANDAC: THANK YOU SO MUCH, DR. CHEN.  
13 MARK, THERE ARE NO ADDITIONAL HANDS RAISED. BACK TO  
14 YOU.

15 CHAIRMAN FISCHER-COLBRIE: GREAT. I THINK  
16 IT'S IMPORTANT FOR US TO TAKE INTO CONSIDERATION THE  
17 COMMENTS FROM THE PUBLIC IN THE ONGOING ASSESSMENT  
18 OF THE PROGRAM AND THE PROCESS. AND WE WILL  
19 CONTINUE TO EVALUATE THE IMPORTANT FEEDBACK AND  
20 CONSIDERATIONS AS WE GO THROUGH THIS EFFORT. AND WE  
21 WILL FOLLOW UP INTERNALLY WITH THE CIRM TEAM AROUND  
22 THAT PROCESS, AND THERE WILL BE FURTHER DISCUSSION  
23 ABOUT HOW WE MOVE FORWARD.

24 ROSA, I DON'T KNOW IF YOU WANT TO ADD SOME  
25 ADDITIONAL COMMENTARY TO THAT.

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1 DR. CANET-AVILES: NO. THANK YOU, MARK.

2 CHAIRMAN FISCHER-COLBRIE: OKAY. THANK  
3 YOU VERY MUCH. WE APPRECIATE THE FEEDBACK. AND  
4 UNLESS THERE ARE ANY OTHER COMMENTS, I THINK WE CAN  
5 CONCLUDE THE MEETING OR ANY OTHER COMMENTS OR  
6 FEEDBACK? OKAY. THERE BEING NONE, I APPRECIATE  
7 EVERYBODY'S TIME. AND WE ARE EXCITED ABOUT  
8 CONTINUING TO TRY TO MAXIMIZE THE OPPORTUNITIES FOR  
9 LEVERAGING AND ACCELERATING SCIENCE. SO WE LOOK  
10 FORWARD TO WORKING HARD AS ALWAYS TO ACHIEVE THAT  
11 GOAL. SO THANK YOU.

12 VICE CHAIR BONNEVILLE: THANK YOU,  
13 EVERYONE.

14 (THE MEETING WAS THEN CONCLUDED AT 2:14 P.M.)

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REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE VIRTUAL PROCEEDINGS BEFORE THE SCIENCE SUBCOMMITTEE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON JANUARY 14, 2026, 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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