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Subject: [EXT] RE: Written Public Comment to REGULAR MEETING OF THE PRESIDENTIAL SEARCH SUBCOMMITTEE OF ICOC CIRM

Dec. 7, 2023

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Written Public Comment to REGULAR MEETING OF THE PRESIDENTIAL SEARCH SUBCOMMITTEE OF THE INDEPENDENT CITIZENS OVERSIGHT COMMITTEE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE Organized Pursuant To The CALIFORNIA STEM CELL RESEARCH AND CURES ACT on Dec 12, 2023

Dear PRESIDENTIAL SEARCH SUBCOMMITTEE of ICOC CIRM,

Thanks for the meeting notice and thank you for this opportunity to present my Public Comment. I'd like to make a public comment regarding your KEY SELECTION CRITERIA FOR PRESIDENT:

"The State of California is an equal opportunity employer" as shown in your exhibit. And your presentation also shows that "CIRM has launched its 5-year strategic plan with a commitment to serve underrepresented communities as well as racially and ethnically diverse populations. To advance our mission and enhance the quality of our programs, DEI must be systematically integrated into CIRM's ecosystem, including both our existing and upcoming programs as well as internally within our organization." However, CIRM updated key selection criteria for President have violated nor only the equal opportunity employer law of the State of California, but also CIRM's own commitment to DEI by using discriminative and marginalizing selection languages or criteria unrelated to CIRM's mission, pursuing California stem cell research and

cures act, to serve as systemic barriers to equal opportunity and fair competition for CIRM President, such as "a medical or scientific unit or organization with a budget of at least $100 [X] million and 200 [X] employees; experience reporting to a board of directors; etc", which systemically deny equal opportunity and fair competition, and serve as insurmountable and discriminative barriers to small businesses, woman-owned small businesses, minority-owned small businesses, racially and ethnically underrepresented communities, economically disadvantaged businesses or communities, economically disadvantaged woman-owned businesses, minority communities, even non-profit research institutes. CIRM is organized to pursue California stem cell research and cures act with California taxpayer dollars, such systemic racism/inequality/discriminative language or criteria or barriers should not be included in the selection criteria for CIRM President. It is also conflict of interest (COI) for CIRM Presidential Search Committee members to use such biased and systemic racism/inequality/discriminative criteria to give their own organizations or their own big Company/Pharm preferential treatment for CIRM President selection, while marginalize small, racially and ethnically underrepresented, economically disadvantaged businesses and communities against CIRM's own DEI policy. CIRM Presidential Search Committee members should not continue to adopt CIRM former President biased and failed hiring policy against the equal opportunity employer law of the State of California to only hire their own close ties who have little or no experience in stem cell research and regeneration, and no knowledge, skill, and qualification for CIRM's mission to pursue California stem cell research and cures act, which has resulted in widespread mismanagement of CIRM grant applications, awards, and portfolio, and massive misappropriation of California taxpayer dollars that have eventually led to her resignation.

As shown in your exhibit, CIRM was created and has been sustained by CA propositions to support the California Stem Cell Research and Cures Act as an established institute that will use the proceeds of bonds to support stem cell research, as well as other related, vital medical technologies for the development of life-saving regenerative medical treatments and cures. CIRM President manages the scientific aspects of CIRM grants applications and awards, which requires he/she to have broad scientific knowledge, vision valuable to CIRM's mission to pursue the California Stem Cell Research and Cures Act, scientific credibility, exceptional leadership skills in stem cell research and regenerative medicine, and unassailable integrity, in order for CIRM to gain public support and voter approval for bond financing to sustain CIRM operations, to fund the best stem cell research, to avoid frauds and wastes of taxpayer money, scandals, and negative public perception of CIRM. Scientific knowledge, vision, leadership skills can only be gained from training and experience. However, in nowhere of the CIRM updated key selection criteria for President, such crucial selection criteria for experience and expertise in stem cell research and regenerative medicine can be found as a qualification for CIRM President. At least 10 years of extensive experience in stem cell research and regenerative medicine, particularly in human embryonic stem cell (hESC) research that CIRM is compelled by California voters to pursue and is crucial for CIRM's mission and success, and expertise in stem cell therapy product

and platform development should be a must for the CIRM key selection criteria for President. And lesson from CIRM former President Maria Millan's resignation also shows how the scientific background and expertise of CIRM President in stem cell research and regenerative medicine is crucial for CIRM's mission and success, and should be a key selection criterion for the next CIRM President in order to restore CIRM's credibility and public confidence in CIRM.

CIRM former President Maria Millan (CIRM President) has only minimal background or little experience in stem cell research. Those grant applications selected by CIRM President/Staff for full review and awards also demonstrate how unbelievably ignorant she was to not only sciences and facts but also what was happening in the biomedical research and biotech real world. Her lack of experience, expertise, leadership, vision in stem cell research and regenerative medicine has resulted in widespread mismanagement of CIRM grant applications, awards, and portfolio, and massive misappropriation of California taxpayer dollars, which have eventually led to her resignation. During her term as CIRM President, CIRM has misappropriated > $300 M to induced pluripotent stem cells (iPSC) that are in fact cancer cells or adult cells reprogrammed with oncogenes or reprogrammed cells (the scientific term of cancer is actually reprogramming), an adult stem cell Ponzi scheme created by the opponents of hESC research during the Bush Administration, to make and bank cancer cells – iPSC -- that are falsely called stem cells, to turn the universities of a "Blue" State into the notorious waste hubs of a scarlet "Red" adult stem cell Ponzi scheme of the Bush Administration and the training centers for the next generation of adult stem cell Ponzi scammers, to fuel the political power and public policy shift to the "Red", which has resulted in the widespread, negative public perception of CIRM and stalled CIRM's bond financing with the State. As a result of her misleading in stem cell research for CIRM, after almost 2 decades later, after 4 or 5 billions of CA taxpayer money later, California still has no clinical-grade hESC lines and banks, no world-class hESC training courses and training centers, no cutting-edge stem cell centers, no highly promising hESC product in clinical trials, no promising treatment or cure for any disorders that destroy lives, though technology has become available. In addition, she also violated CIRM conflict of interest (COI) rule to misappropriate ~$55 M to her former Stanford mentor Irving Weissman's Company Forty-Seven and Stem Cell that have produced absolutely nothing for California taxpayers, but at least $67 million profit for Stanford and $191 million profit for Irving Weissman, besides their cover up of Stanford's ~$15 million payment to the State as "loyalty payment". If you go to CIRM grants search, you could see the CIRM funding or California taxpayer money to Forty-Seven and Stem Cell has been reset to $0, which might give you some idea why CIRM former President Maria Millan resigned.

CIRM former President Maria Millan also only hired CIRM General Counsels and staff of their close ties who have not only minimal background or little experience in stem cell research, but also have absolutely no knowledge, skill, and qualification for the jobs of CIRM grants review or portfolio development, such as Linda Nevin, Senior Science Officer for Grant Review at CIRM, Hayley Lam, Associate Director, Portfolio Development & Review at CIRM, CIRM General

Counsel Rafael Aguirre-Sacasa. As a result, CIRM President/Staff could not even provide clear and easy-to-understand guidelines and instructions for grant application packages. As a result, there are widespread mismanagement in CIRM grant selection, review, and award; irresponsiveness of CIRM President/Staff to applicant's questions about their very confusing grant application packages and eligibility forms; irresponsiveness of CIRM President/Staff to frauds and wastes of taxpayer dollars even after those scandals have come to light; which have resulted in widespread negative public perception of CIRM and severe damages to CIRM's credibility and public confidence in CIRM. For example, CIRM President/Staff continued to only select iPSC applications of their close ties to full review and CIRM award even after CIRM President's cover up of Stanford's ~$15 million payment to the State as "loyalty payment"; CIRM President/Staff continued to select iPSC clinical trial awards, including the one to UCLA, even after iPSC had generated cancers and failed all safety trials; CIRM President/Staff continued to select immunotherapy/cytokine-therapy applications and immuno-oncology companies for full review and awards even after Forty-Seven/Gilead Sciences had failed their clinical trial, and even after the widespread clinical trial failures of immune-oncology companies in the biotech world.

As a result, almost no CIRM DISC2 awards selected by CIRM President/Staff for full review could progress to CIRM TRAN, and almost no CIRM TRAN awards selected by CIRM President/Staff for full review could progress to CIRM CLIN. Although CIRM eligibility criteria clearly say, to be eligible for CIRM Application and Awards: "human stem or progenitor cells either comprise the product/tool or are used to manufacture the product/tool", and technically and scientifically, the reprogrammed/cancer cells iPSC are not even stem cells, not even meet the eligibility criteria of CIRM applications, CIRM President/Staff still would only select and continue only select iPSC fraud and waste applications, but not hESC applications that completely meet CIRM eligibility criteria and pursue California stem cell research and cures act, to full review and for CIRM awards, like CIRM TRAN awards to Defined Biosciences of UCSD stem cell center director Alysson Muotri and HEALIOS NA of Japan that are directly linked to CIRM President in the last round, and many CIRM iPSC awards before. CIRM eligibility criteria clearly say, to be eligible for CIRM Application and Awards, the organization or company needs to be in California. It is outrageous that CIRM President/Staff do not select/fund California organizations and companies that already have innovative defined technology to derive and maintain clinical-grade pluripotent stem cell lines for research and therapies in order to find treatments and cures as compelled by California voters, instead gives California taxpayer dollars to a Japanese Company directly linked to CIRM President to waste on making cancer cells/reprogrammed cells – iPSC -- that are falsely called stem cells, and those big Company/Pharms outside California that do not even meet CIRM application eligibility, like the $15 million to the eye Secretome of Combangio, a subsidiary of Kala Bio, Bob Langer of MIT's Company.

In regenerative medicine, human embryonic stem cell (hESC) research holds huge promise for treating major human diseases that have been challenging for traditional medicine, such as a wide range of incurable or hitherto untreatable neurological and heart diseases. Millions of people are pinning their hopes on hESC research. However, despite that hESC research innovations could provide urgently-needed life-saving treatments or cures for major health problems that affect millions and cost trillions, the science or scientific, format, and eligibility criteria aspects of CIRM guidelines and instructions for grant application packages set by former CIRM Presidents/Staff have prevented the most translational research – human embryonic stem cell research -- from translating to clinics, as CIRM has done in almost 2 decades.

The science or scientific, format, and eligibility criteria aspects of CIRM guidelines and instructions are unclear or confusing or biased. It is very obvious that CIRM guidelines and instructions are formatted and written for adult stem cell research & therapy applications, genetic or gene therapy applications, biologics or drug applications, but not for hESC research and therapy applications, which has made it very hard for hESC research and therapy applicants, including the scientific terms, eligibility criteria, and application formats of CIRM guidelines and instructions, which all are the scientific terms, technical requirements, and formats for adult stem cells, adult stem cell therapy, genetic or gene therapy, drugs or biologics, not suitable hESC research and therapy. After almost a year since the FDA Modernization Act 2.0 was enacted into law to legitimize alternatives to animal testing for advancing a drug or product to human trials, CIRM TRAN still requires "preclinical animal model data relevant to the target clinical indications" to even apply, even though most of CIRM TRAN awards only have failed "preclinical animal model data relevant to the target clinical indications" that have failed to demonstrate the efficacy in their animal models, e.g., failed animal data that have failed to regenerate, repair, or replace the diseased or damaged tissues or organs. Preclinical animal model data provide little implication for human trials. Companies use tens of thousands of animals for animal tests each year. Yet more than nine in 10 drugs that enter human clinical trials fail because they are unsafe or ineffective. Unlike traditional R&D, hESC-based therapeutic products have been developed directly with human cells with proof-of-concept already established in humans, which makes preclinical animal studies totally meaningless, unnecessary, and waste of time. The only role that CIRM TRAN requirement of "preclinical animal model data relevant to the target clinical indications" set by the very ignorant former CIRM Presidents/Staff serves is to prevent the most translational research – hESC research -- from translating to clinics, stalling CIRM's mission to pursue California stem cell research and cures act.

For example, CIRM guidelines and instructions are actually formatted and written specifically for induced pluripotent stem cells (iPSC) that are in fact cancer cells or adult cells reprogramed with oncogenes (the scientific term of cancer is reprogramming), an adult stem cell Ponzi scheme or scam created by the opponents of pluripotent hESC research, which has made it very hard for hESC research and therapy proposals. In CIRM TRAN, there is only guidelines and instructions for deriving allogeneic (donor-derived) cancer cells – iPSC, but no guidelines and

instructions for deriving any stem cells, such as embryo-derived human embryonic stem cells. CIRM was established and has been sustained by CA propositions with taxpayer money to pro, but not con hESC research by funding hESC research and therapy applications in order to find treatments and cures for a host of disorders that destroy lives. CIRM President/General Counsel/Staff should not align with the opponents of hESC research, should not use the terms and requirements/formats of the opponents of hESC research in CIRM guidelines and instructions to make it very hard for hESC research and therapy applicants, and should not give the opponents of hESC research and their Ponzi scheme or scam preferential treatment in grant applications that has led to the massive fraud and waste of taxpayer dollars.

For example, CIRM guidelines and instructions use the very biased or restrictive scientific terms of autologous and allogeneic stem cells, transplantations, and therapies that are only for adult stem cells, particularly referring to haematopoietic stem cells and mesenchymal stem cells, but not for embryonic stem cells. And "human embryonic stem cell" is not even in the stem cell key word of CIRM guidelines and instructions, considering the uniqueness and resourcefulness offered by hESC to therapy and science that no other stem cells can, and that California voters have passed 2 propositions to fund. Instead CIRM guidelines and instructions use the very confusing word "pluripotent stem cell" as the stem cell key word, as though CIRM has consented to the opponents of hESC research that "hESC and iPSC are identical". CIRM guidelines and instructions only consider the ethical issue, informed consent, good tissue practices (GTP) of adult cell/tissue donors for iPSC, but completely ignore the ethical issue and informed consent of embryo donors for hESC. And CIRM TRAN only have guidelines and instructions for Allogeneic Cell Derivation or adult cell derivation or cancer cell derivation from cell or tissue donors, specifically for iPSC, but no guidelines and instructions for human embryonic stem cell line derivation from embryo donors.

For example, CIRM guidelines and instructions say "CIRM considers regenerative medicine to mean therapeutic approaches that are intended to replace, regenerate or repair the function of aged, diseased, damaged or defective cells, tissues, and/or organs", which is very unclear and confusing. In fact, CIRM has funded no awards that could provide any therapeutic approaches to replace, regenerate or repair the function of aged, diseased, damaged or defective cells, tissues, and/or organs. Most adult stem cells or almost all CIRM awards only provide protective mechanism that has no clinical benefit and efficacy, but not graft-dependent replacement or regeneration. None of CIRM awards have demonstrated the capability of their stem cell (e.g., iPSC, CSC, NSC) to generate a large supply of vital functional cells (e.g., neurons, cardiomyocytes) to replace, regenerate or repair the function of aged, diseased, damaged or defective cells, tissues, and/or organs (e.g., spinal cord, brain, or heart) in order to have clinical benefit and efficacy to address the unmet medical need. hESC overcome such limitations of adult stem cells to provide graft-dependent replacement or regeneration mechanism, clinical benefit and efficacy, and therapeutic approaches that could replace, regenerate or repair the function of

aged, diseased, damaged or defective cells, tissues, and/or organs. Traditional drug development usually starts with drug leads discovered in non-human simple model organisms, thus requires lengthy and costly both demonstration in animal model testing and establishment of proof-of-concept and safety in human trials. As a result, millions of drug leads have vanished before even reach clinical trials, and for few lucky ones, have encountered the very high drug failure rate in human trials. Among those very few drugs that eventually obtained their market approvals, there were not any cures, or even meaningfully effective treatments for a host of disorders that destroy lives. Unlike traditional R&D, hESC-based therapeutic products have been developed directly with human cells with proof-of-concept already established in humans, which simplifies the development process, lowers the costs, shortens the time consumption, and increases the probability of clinical success dramatically. Cell therapy products have very different benchmarks or indicators regarding to safety and efficacy, which makes CIRM guidelines and regulations in CIRM TRAN and CLIN typically for conventional drug or biologic development obsolete and not suitable for stem cell therapy applications. The safety of a human stem cell therapy product is evaluated NOT by toxicity, but by whether it can retain a stable phenotype and karyotype for a long period of time and whether there is no tumor, inappropriate cell type formation, or abnormal regeneration. The efficacy of a human stem cell therapy product is measured by its cellular ability to regenerate the tissue or organ that has been damaged or lost, but NOT by the chaperone activity of traditional stem cells to produce trophic or protective molecules to rescue endogenous host cells that can simply be achieved by a drug of molecular entity.

For example, CIRM DISC eligibility requirement “advance the application of genetic research as it pertains to stem cells or regenerative medicine” and CIRM instructions even specify that “CIRM considers that genetic research to mean research that alters genomic sequences of cells (edit, remove, or add DNA sequences) or introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells”, which are scientific terms unequivocally referring to iPSC, gene editing/Crispr or gene therapy, but make hESC research actually ineligible for CIRM funding, even though hESC research offers great genetic insights to bridge the knowledge gaps of human development critical to fight diseases.

CIRM President/Staff using such biased or restricted scientific terms in CIRM guidelines and instructions has resulted in biased grant selections and awards towards adult stem cells, genetic or gene therapies, and even adult stem cell Ponzi schemes and scams, biasing against hESC research and therapy, and biasing against CIRM own mission that is compelled by CA voters and propositions to fund hESC research and therapy with CA taxpayer money. To avoid fraud and waste, CIRM guidelines and instructions should specify the eligibility criteria that the proposed stem cells have demonstrated the capability to generate a large supply of vital functional cells (e.g., neurons, cardiomyocytes) to replace, regenerate or repair the function of aged, diseased,

damaged or defective cells, tissues, and/or organs (e.g., spinal cord, brain, or heart) in order to have clinical benefit and efficacy to address the unmet medical need.