CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Independent Citizens' Oversight Committee
From: Jim Campanelli, Ph.D. & Lisa McGinley, Ph.D., Senior Science Officers Preclinical Development; Shyam Patel, Ph.D., Associate Vice President Preclinical Development; Rosa Canet-Avilés, Ph.D., Chief Science Officer
Re: RAPID Concept Plan
Date: January 29, 2026

The proposed Rare Disease Acceleration Through Platform Innovation and Delivery (RAPID) Concept Plan is part of the second implementation phase of the Strategic Allocation Framework (SAF), which was approved by the ICOC in September 2024. This new concept plan supports platform-based approaches to accelerate development of rare disease therapies toward FDA approval.

I. Background: Genetic Therapies for Rare Diseases

It is estimated that there are over 10,000 rare[1] diseases that collectively afflict 1 in 10 Americans, and ~80% of these diseases have a genetic basis. While the vast majority of currently approved genetic therapies are targeting rare diseases, it is estimated that 95% of rare diseases have no approved therapy[2]. The traditional approaches to development, approval, and commercialization of therapies are not amenable to addressing the large number of genetic diseases that each affect a relatively small number of patients.

Funders, regulators, drug developers, clinicians and patient advocacy organizations have all recognized the need for alternative approaches to enable more rapidly available and affordable therapies for patients with rare diseases. One such approach is platform-based genetic therapies. Platforms are comprised of common sets of technologies that can be leveraged for accelerated and resource-efficient development, manufacture, clinical delivery and regulatory review of multiple related therapies. For example, a CRISPR gene therapy composed of three components (DNA editor, guide RNA and lipid nano-particle delivery vehicle) is a platform in which switching just one component (e.g. the guide RNA) could target different genetic disease-causing mutations: be it one gene with many mutational variants (e.g. Phenylketonuria [PKU]), or one pathway with several genes (e.g. Urea Cycle Disorders [UCD]), or one process with several pathways (e.g. lysosomal storage disorders).

By leveraging the collective safety and efficacy datasets with the components of the platform, it should be faster and cheaper to advance the next therapy to the clinic when only a single component, i.e. the guide RNA, has been changed. Recent actions by the FDA (including draft

[1] CIRM defines rare disease as a disease with a prevalence of <200,000 patients in the US
[2] *Looking for the Common in Rare*. (2024, July 21). Global Genes. https://globalgenes.org/raredaily/looking-for-the-common-in-rare/

platform designation guidance[3]), scientific workshops on platform gene therapies[4], and publication of the plausible mechanism pathway[5], together suggest a pathway for rapid, resource-efficient development and approval of multiple genetic therapies for multiple related indications.

A team of NIH-funded researchers from Children's Hospital of Philadelphia recently pioneered an approach for rapid development and delivery of a genetic base-editing therapy for Baby KJ[6]. This team has further leveraged this approach, based upon the principles above, and received FDA agreement in pre-IND interactions for platform-based genetic therapy development. By leveraging the existing and planned safety & efficacy studies, the team obtained preliminary FDA concurrence on a dramatically streamlined pathway for preclinical development and clinical testing of multiple base-editing therapeutic candidates for multiple genes across two metabolic diseases[7,8].

II. Rare Disease Therapeutic Development at CIRM: the Opportunity

CIRM has a long history of funding the research and development of regenerative medicine therapies for patients with rare genetic diseases. At the December 11th, 2025 ICOC meeting, the Application Review Subcommittee (ARS) approved $160M in new award funding for preclinical and clinical development projects including genetic therapies for patients with rare genetic diseases such as Friedreich's Ataxia, Alpha-1 anti-trypsin deficiency, limb girdle muscular dystrophy, and Dravet syndrome. In each case, a single therapeutic candidate is supported to target one specific indication. To bridge the gap between promise and practice in platform-based therapy development for patients with rare diseases, an evidence base of safety, efficacy, and quality data must be established across multiple genetic therapy platforms for multiple types of rare genetic diseases. The RAPID program aims to foster the technical and regulatory innovations that will be required to achieve the vision of rapid development, delivery, and accessibility of genetic therapies to patients with rare diseases based upon platform technologies.

III. RAPID Program Design

The objective of the RAPID program is to create scalable models that can rapidly deliver transformative platform-based genetic therapies to patients with rare diseases. The RAPID Program utilizes existing structures of CIRM's Preclinical Development (PDEV) and Clinical Development (CLIN2) funding programs but is designed to encourage and support in vivo genetic therapy projects that propose parallel progression of multiple therapies with streamlined testing requirements, reduced capital and operational costs through shared components and

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[3] Center for Drug Evaluation and Research (2024, May 29). *Platform Technology Designation Program for Drug Development*. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/platform-technology-designation-program-drug-development

[4] Fyodor Urnov, Kassim, S., Kiran Musunuru, Liu, D., Lee, A., Barrera, L., Stetkiewicz, P., Bruno, J., Hewitt, M., Lister, T., Malech, H., Gasch, L., Diver, M., Gertler, N., Grignon, F., Le, A., Lehmicke, M., Almendro-Navarro, V., & Lembong, J. (2025). *Advancing gene-editing platforms to improve the viability of rare-disease therapeutics: Key insights from a 2024 Scientific Exchange hosted by ARM, ISCT, and Danaher*. Cytotherapy. https://doi.org/10.1016/j.jcyt.2025.06.010

[5] Prasad, V., & Makary, M. A. (2025). *FDA's New Plausible Mechanism Pathway*. New England Journal of Medicine. https://doi.org/10.1056/nejmsb2512695

[6] Musunuru, K., Grandinette, S. A., Wang, X., Hudson, T. R., Briseno, K., Berry, A. M., Hacker, J. L., Hsu, A., Silverstein, R. A., Hille, L. T., Ogul, A. N., Robinson-Garvin, N. A., Small, J. C., McCague, S., Burke, S. M., Wright, C. M., Bick, S., Indurthi, V., Sharma, S., & Jepperson, M. (2025). *Patient-Specific In Vivo Gene Editing to Treat a Rare Genetic Disease*. New England Journal of Medicine, 392(22). https://doi.org/10.1056/nejmoa2504747

[7] Ahrens-Nicklas, R., Musunuru, K. (2025). *How to create personalized gene editing platforms: Next steps toward interventional genetics*. The American Journal of Human Genetics, Volume 112, Issue 12, 2826 – 2829

[8] Somatic Cell Genome Editing (SCGE) Platform. *SCGE Shared Regulatory Documents* (2025). https://scge.mcw.edu/platform/public/documents/regulatory

development pathways, and build a cumulative evidence base that enhances regulatory confidence and accelerates future approvals.

The RAPID program will fund two types of awards to achieve its objective: RAPID Validation and RAPID Innovation.

RAPID Validation - Validation awards are intended for projects that have already engaged with the FDA and received preliminary regulatory alignment on their platform approach via a pre-IND[9] meeting. Validation awards will support all activities required to initiate and complete a first-in-human (FIH[10]) master protocol[11] clinical trial for a basket of genetic therapy candidates. By accelerating these projects through IND-enabling studies and clinical proof-of-concept, the Validation awards will directly test principles of the platform-based genetic therapy development approach and the tenets of the plausible mechanism pathway.

Examples of RAPID Validation projects may include non-viral liver-directed gene editing therapies for metabolic diseases or AAV[12] genetic therapies for neurodevelopmental disorders, where current genetic therapy technologies can be leveraged to efficiently target multiple rare diseases.

RAPID Innovation - These projects are expected to push the boundaries of what constitutes a platform, including innovations that could reduce testing requirements or expand applicability across multiple rare diseases. Applicants must have completed or have requested an FDA INTERACT[13] meeting at the time of application. The expected outcome for Innovation awards is IND clearance, supported by early regulatory engagement, thereby de-risking the development path.

Examples of RAPID Innovation projects may include CNS genetic therapies that incorporate novel non-viral delivery technologies or next-generation gene editing technologies that leverage novel *in vitro* testing models and analytical assays.

IV. Novel Program Features

Considering the rapidly evolving regulatory landscape and technology advancements, in combination with the dynamic nature of RAPID-funded projects, this program incorporates several features that contrast with our existing PDEV and CLIN2 funding opportunities. The design and rationale for these features are based on CIRM's experience managing preclinical and clinical development programs as well as feedback from genetic therapy experts and funders.

Award Cap - The Validation and Innovation awards will solicit a range of proposals across different genetic technologies, disease areas, and stages of development, with the expectation of efficiencies resulting in a combination of time and cost savings. Each program will be required to propose and justify how their platform-based approach minimizes time and cost to therapeutic availability and the extent to which such efficiencies translate to future additional variants and indications. Given the range of possible approaches and paths to regulatory innovation, it is not

[9] IND: Investigational New Drug
[10] FIH: First-in-Human
[11] A master protocol is a clinical trial protocol designed with multiple coordinated sub-studies to evaluate one or more investigational drugs for one or more diseases within the overall trial structure
[12] AAV: Adeno-associated virus
[13] INTERACT: Initial Targeted Engagement for Regulatory Advice on CBER/CDER Products

feasible to define a singular award cap for either type of award category. However, CIRM will provide its expectation for number of awards to be funded with the available program budget. Applicants will be expected to propose competitive projects that demonstrate platform-based efficiencies and maximize potential for clinical impact within a well-justified budget.

RAPID applications will undergo CIRM budget review and award funds will be disbursed contingent upon achievement of milestones utilizing existing award management mechanisms. The amount of total project costs requested must be adequately justified and is subject to adjustments prior to issuance of an award based upon assessments of the Grants Working Group (GWG), the CIRM team, or by the Application Review Subcommittee (ARS) of CIRM's Governing Board.

Minimum Required Co-Funding - The PDEV and CLIN2 programs require minimum co-funding for for-profit awardees and non-profit awardees with for-profit partners. In recent years, there has been a substantial pullback in industry support for rare disease genetic therapy development. This is due to several factors including the cost of developing rare disease therapies and challenges in commercialization. To help reduce funding-based barriers for potentially impactful RAPID proposals and to demonstrate its commitment to funding ambitious solutions to the unmet medical needs of patients with rare diseases, the RAPID program will not require a minimum co-funding amount. However, applicants will be highly encouraged to secure voluntary co-funding, in-kind funding, and in-kind resources to help advance RAPID-funded projects to the expected award outcome. Applicants will also be required to commit contingency funding to cover anticipated project risks.

Supplemental Funding - Feedback from other funders stressed the need for flexibility in supporting novel platform-based approaches. Given that the scale and scope of the project is predicated on regulatory advancements and emerging data, supplemental funding may enable necessary responsiveness of otherwise well-performing projects.

For the RAPID program, CIRM will reserve an initial $5M in program funding for CIRM to deploy on accelerating RAPID awards at key inflection points. CIRM proposes that, upon achievement of distinct project milestones, awardees may request supplemental funding to accelerate the project, subject to availability of RAPID program funds and CIRM approval. Supplements are not guaranteed, must be adequately justified, and may only be requested at designated points in the award. For example, upon successful completion of a pre-IND meeting milestone, a RAPID Innovation award may have a need to expand an IND-enabling study to respond to FDA feedback. In the case of a RAPID Validation award, upon IND clearance, the project may have the ability to advance additional candidates to reach more patients in the master protocol trial.

Program Budget - CIRM proposes an initial total program budget allocation of $100M to be deployed over two annual application cycles over the next two fiscal years: an allocation to allow sufficient time and resources to accommodate emerging technological advancements and evolving regulatory frameworks essential to RAPID objectives.

- FY 26-27: CIRM proposes to allocate $55M in research funds to the RAPID program. Of the $55M, $5M will be reserved as program supplement to be deployed as described above over the lifetime of the program. With the remaining $50M, CIRM expects to fund 2-3 awards in the annual FY 26-27 application cycle.
- FY 27-28: CIRM proposes to allocate $45M in research funds to the RAPID program. It is currently anticipated that the entirety of the $45M will be directed toward 2-3 new awards in the annual FY 27-28 application cycle.

- Future Years: Given the dynamic nature of RAPID awards, CIRM award funds may be recovered as part of standard CIRM award management operations. If enough RAPID funds are recovered, CIRM may request ICOC approval to replenish the supplement reserve or to open an additional funding cycle as part of the fiscal year research budget proposal.

Knowledge Network & Data Sharing - To help broadly advance platform-based development of genetic therapies, the RAPID program will incorporate requirements for near real-time knowledge sharing within the CIRM awardee network as well as timely public sharing of data and knowledge. This structured approach to knowledge sharing introduces clear requirements and timelines that go beyond other CIRM funding programs to achieve the goal of accelerating collective learning and regulatory alignment. For example, sharing of study designs, emerging data and regulatory strategies within the CIRM awardee network may help RAPID projects as well as other CIRM projects align and coordinate testing and regulatory strategies across related genetic therapies. Similarly, public sharing of FDA feedback within 6 months of a pre-IND meeting helps ensure that other projects, whether CIRM-funded or not, collectively benefit from the learnings and build the evidence base for platform-based genetic therapy development.

V. Request for Action

We seek ICOC approval of the proposed RAPID Program Concept, with an initial allocation of $100M in the first two funding cycles (FY2026-2027 and FY2027-2028).