

Memorandum

To: Members of the Independent Citizens' Oversight Committee
From: CIRM Team
Re: Strategic Assessment of CIRM's Clinical Portfolio
Date: September 24, 2026

Executive Summary

CIRM has built a substantial clinical portfolio and is making meaningful progress toward its Strategic Allocation Framework (SAF) goals. 1 CIRM-supported therapy has received Biological License Application (BLA) approval, 4 programs have submitted or are preparing to submit BLAs, and 7 are in pivotal development or continue to progress towards it. All 11 are progressing with external support, showing that CIRM's investment helped de-risk the programs enough for others to carry them forward. The September discussion builds on that progress and asks what role CIRM should play in clinical development as the portfolio matures.

CIRM has approximately \$1.054 billion in currently uncommitted clinical-development program funding projected over 8 years beginning in FY 2026-27. To inform upcoming programmatic decisions, the CIRM Team recommended providing the Board with a review of the clinical portfolio, and the Board agreed. The review began with the assumption that CIRM might need to fill late-stage funding gaps as programs matured. As the analysis progressed, the picture became more nuanced. Some programs are advancing toward late-stage development without additional CIRM funding. Others have reached meaningful stages of development but remain dependent on CIRM for much larger investments that may still leave the path to patients unresolved. The issue is no longer simply how far CIRM should fund an individual program. It is what role CIRM should play in clinical development, and where CIRM's investment can make the greatest difference for patients.

The CIRM Team recommends a staged approach to clinical funding. CIRM would take more risk early to broadly de-risk programs and create credible paths for continued development. As programs mature, CIRM would fund alongside others when shared risk can move a promising therapy to a meaningful inflection point, while other parties would carry most of the remaining pivotal, BLA-enabling, and commercialization risk. This approach would preserve CIRM's flexibility without making it the continuing primary

funder of the remaining pathway. The CIRM Team requests approval of this direction in September and will return in December with the related program and review updates.

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I. Background

Strategic Framework

CIRM's clinical funding is intended to move promising therapies toward patient impact. Funding programs are a means of fulfill that mission. Regulatory approval is an important milestone, but the ultimate objective is for therapies to be launched, made accessible to Californians, and reach patients.

Two goals of the Strategic Allocation Framework are especially relevant to this objective. Goal 3 calls for advancing 4 to 7 rare disease projects to BLA. Goal 4 calls for moving 15 to 20 therapies targeting diseases affecting Californians into late-stage trials. Together with Proposition 14's accessibility and affordability mandate, these goals reflect CIRM's ultimate objective, which is to ensure that promising therapies reach patients.

The goals define some the outcomes that CIRM seeks, but they do not determine how much of the development pathway CIRM should finance. They also do not answer what CIRM should do when a program reaches a stage where the cost and risk increase substantially.

How the Question Changed

To inform upcoming programmatic decisions, the CIRM Team began a review of the clinical portfolio. The review began with an assumption that CIRM might need to fill late-stage funding gaps as programs matured. One of the initial questions was whether CIRM should develop a new funding mechanism for programs approaching pivotal development and BLA.

The historical portfolio shows substantial progress and external validation. CIRM has supported 127 clinical trial-stage awards covering 121 trials and 112 unique clinical programs. About half of those programs appear to have attracted venture or public-market financing, and approximately 11 active programs currently have potential commercialization capacity.¹ These measures are encouraging, but they do not establish that funding is committed to the CIRM-supported therapy or that a sponsor can carry it through launch and patient access. Appendix 1 explains the distinction among awards, trials, and clinical programs.

As the analysis progressed, the picture became more complicated. The CIRM Team began looking more broadly at which programs continued after CIRM funding, what prevented others from advancing, and whether further CIRM investment would materially improve the likelihood that a therapy reaches patients.

What the Portfolio Reveals

The portfolio review shows different outcomes following initial CIRM-funded clinical development. Some programs generate enough evidence and value for another organization to continue development. CIRM remains engaged on access, California impact, and portfolio learning without continuing as the primary funder. Other programs reach meaningful stages of development but do not yet have a viable path forward. Advancing these programs would require CIRM to assume substantially more of the remaining development burden.

This distinction has significant implications for CIRM's remaining clinical funding. CIRM has approximately \$1.054 billion projected for clinical development over the next 8 years. Supporting clinical proof-of-concept or another defined inflection point would allow CIRM to invest across a broader portfolio and create more opportunities for programs to attract external support. Funding a substantial portion of the remaining development through BLA would concentrate those resources in far fewer programs and leave CIRM carrying more of the development risk.

A large investment through BLA may also leave the path to patients unresolved. After BLA, a therapy still requires a capable organization and sufficient resources for manufacturing, launch, reimbursement, treatment delivery, and patient access.

The question for CIRM is therefore broader than whether to fund the next study or fill a late-stage funding gap. What role should CIRM play as programs mature and where can its funding have the greatest impact for patients? Should CIRM continue as the primary funder through late-stage development and BLA?

¹ External capital and commercialization capacity do not guarantee BLA submission, BLA approval, commercial launch, or patient access. Company financing does not mean that the capital will be committed to a CIRM-supported asset, such as when the company has a different lead asset.

The 112 historical clinical programs provide context for understanding what occurred during and after CIRM funding. For this forward-looking assessment, the CIRM Team focused on 53 active clinical-stage programs and 6 programs associated with closed awards that continue to advance through clinical development, pivotal or BLA-related activity, or another confirmed development path. Programs that were terminated or had no known active path remained part of the historical portfolio but were not included in this assessment.

The CIRM Team organized the 59 programs into 3 groups based on their current development path and anticipated need for additional CIRM funding:

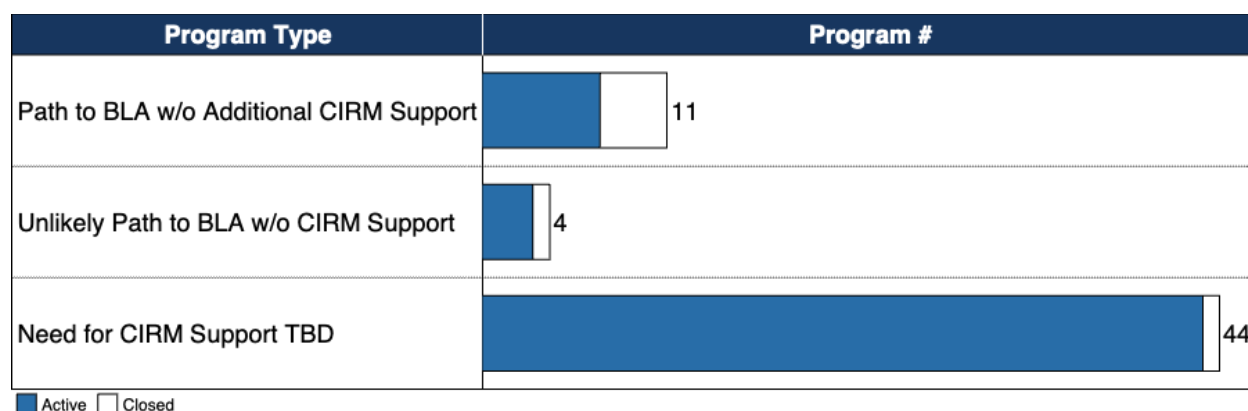


Figure 1. Clinical-stage programs by development path and expected need for additional CIRM funding (data as of August 2026).

Programs with a path to BLA without additional CIRM funding. CIRM supported the earlier clinical development of these programs, helping generate the evidence needed to advance. Other organizations have since assumed the primary funding and development role through additional investment, partnership, acquisition, or continued sponsor support. These programs span different diseases and therapeutic approaches and have confirmed ongoing development toward BLA. Their progress shows how CIRM’s early investment can help position a program for others to carry forward.

Programs unlikely to reach BLA without substantial additional CIRM funding. CIRM has already supported significant development of these programs, in some cases across multiple stages and into pivotal trials. Despite that investment, they do not currently have external funding or sponsor capacity to complete the remaining development. Further progress would require CIRM to assume a much larger share of the clinical, regulatory, manufacturing, and financial risk. The group is concentrated in rare and ultra-rare diseases and includes several complex autologous gene-modified approaches, where the path to manufacturing, commercialization, and patient access can be particularly challenging.

Programs for which the need for future CIRM funding remains to be determined. This is a mixed group. Some programs are still early and require additional clinical data

before their path can be assessed. Others have shown promise and have a defined next step, but their ability to continue depends on the next outcome and getting financing and/or partnership. A third set is comprised of older programs that face development, enrollment, regulatory, or sponsor-related challenges that make continued progress more difficult. As the evidence and circumstances change, programs may move into the group advancing with external support, move into the group requiring further CIRM funding to advance, or discontinue development.

These groups describe each program's current development path. They are not assessments of scientific merit or predictions of regulatory success. The size of the third group (44 programs with need for CIRM support to be determined) means that CIRM will face these decisions repeatedly over the remaining funding horizon.

The portfolio also reinforces an important distinction between reaching BLA and reaching patients. BLA is an important development milestone, particularly under SAF Goal 3, but it does not by itself address commercial manufacturing, launch, reimbursement, clinical adoption, treatment center readiness, or sustainable patient access. CIRM's clinical portfolio framework recognizes that commercialization and accessibility continue beyond BLA. At that stage, CIRM's contribution extends beyond funding. CIRM works with programs to apply available access and affordability resources and uses their experience to inform support for other therapies.

The question before the Board is therefore broader than how to finance several late-stage programs. It is what role CIRM should play across clinical development as the portfolio matures and where can its funding have the greatest impact for patients.

II. Recommendations

The CIRM Team proposes that CIRM adopt **portfolio de-risking as its default clinical-development role, focusing clinical funding on de-risking broadly and creating credible continuation paths.**

Under this approach, CIRM would continue to provide substantial clinical funding to generate meaningful clinical evidence, resolve important development uncertainties, and support informed decisions about further development. CIRM's funding role would evolve as programs mature and other sources of support become available.

Early in clinical development, CIRM would carry a larger share of the risk to help promising programs establish the evidence needed to advance. Later, CIRM would fund alongside others when shared risk can move a promising therapy to a meaningful inflection point. Other parties would be expected to carry the remaining pivotal, BLA-enabling, and commercialization risk.

De-risking would be assessed by what the funded work accomplishes. Depending on the program, this could include clinical results sufficiently mature by the end of the award to

inform the next development step, clearer regulatory alignment, manufacturing readiness, or resolution of another defined barrier. As programs mature and funding needs grow, CIRM would expect stronger external commitment and greater clarity about who will lead and finance subsequent development.

Trial phase alone would not determine CIRM's role. A Phase 1/2 or Phase 2 study may serve a pivotal or registrational purpose based on its design, intended regulatory use, and FDA alignment. CIRM's funding decisions would depend on what the proposed work can accomplish, how much risk CIRM would carry, and whether there is a credible path for continued development.

This direction would guide future funding opportunities and management of the existing portfolio. It would preserve CIRM's ability to support programs broadly and participate later through shared funding, while avoiding continued responsibility as the primary funder of the remaining development pathway when no durable continuation path has emerged.

This path does not mean that all early-stage clinical programs would be appropriate for CIRM support. Stage alone would not determine fit. CIRM would prioritize programs where a defined investment can generate meaningful clinical or development evidence, address a clear barrier, and position the program for a credible next step. Programs without a sufficiently clear development path, or where the proposed award is unlikely to reach a meaningful decision point or create a realistic path for continued development, may not fit within the revised program.

The current CLIN2 program provides a foundation for this work through its support for trials across phases, co-funding requirements, access and commercialization planning, and scientific and programmatic review. The September action would establish the strategic direction for the CIRM Team to develop proposed refinements.

December Work

If the Board approves the recommended direction, the CIRM Team will return in December with:

Clinical Program Updates

- An updated CLIN2 concept with proposed refinements to its scope and funding approach, clearer expected outcomes for supported programs, and updates to program requirements; and
- A proposal for more structured portfolio visibility and external engagement.

Review Process Updates

- Review approach aligned with the revised clinical funding strategy;

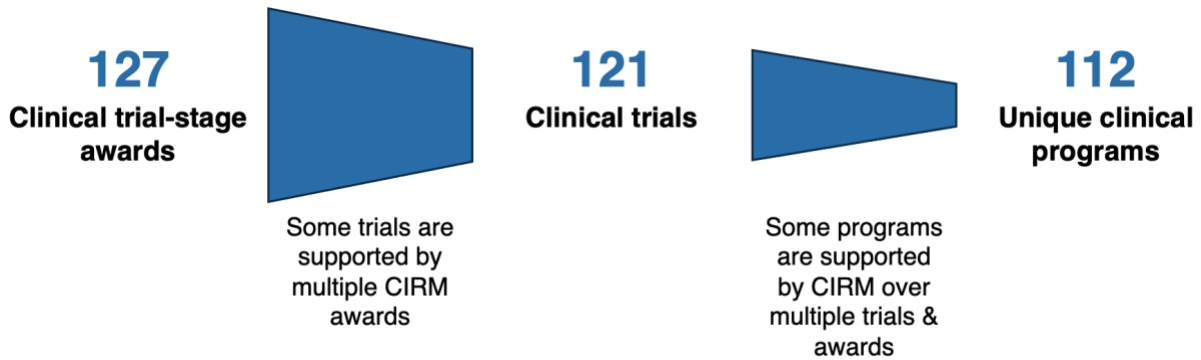
- The revised clinical program concept will define not only the stages CIRM will support, but the characteristics a program must demonstrate to warrant investment, including the expected outcome of the award and a credible path for subsequent development. In December, the CIRM Team will return with proposed funding parameters, program requirements, and review expectations. Following approval of a CLIN2 concept amendment, the Team would develop the revised Program Announcement, applicant resources, consultation process, and review preparations. The current timeline anticipates bringing the first awards under the updated program to the Board in December 2027 (Figure 2).



CIRM requests the ICOC approve these recommendations.

- Appendix 1: Awards, Trials, and Clinical Programs
- Appendix 2: Clinical Portfolio Detail (See Separate Document)

Appendix 1: Awards, Trials, and Clinical Programs



CIRM has supported 127 clinical trial-stage awards covering 121 clinical trials and 112 unique clinical programs. Some trials received funding through more than one CIRM award, and some programs received support across multiple trials and awards. For this assessment, a clinical program is a therapeutic candidate being developed for a specific indication.