Navigating the Path from Capsid Access to IND: A CMC Playbook for Early Gene Therapy Teams

A Practical Perspective from the Developer Side of the Table

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Introduction

Getting access to a next-generation engineered capsid is a significant milestone for an early gene therapy program. What happens next: the chain of CMC, manufacturing, and development decisions between capsid access and a IND submission. This is where programs either build momentum or quietly lose months.

For lean, early-stage teams, these decisions are cross-functional, phase-dependent, and easy to miss. What's often missing is experienced sponsor-side judgment that can translate discovery-stage decisions into a realistic path through CDMO selection, process development, external manufacturing, IND documentation, and potential ex-US regulatory pathways.

This paper offers a practical playbook for navigating that path, drawn from direct experience leading and supporting early-stage gene therapy programs, including a novel capsid program taken from platform concept through FDA-accepted IND with no CMC comments, and current work supporting cross-border AAV programs through PD, manufacturing, and IND strategy.

The CDMO Selection Problem: Cost Is Not Fit

Early-stage teams under pressure to move fast often drive CDMO selection toward the lowest-cost proposal. This is understandable, but it’s also where programs begin to accumulate what I call process debt: suboptimal early decisions with compounding downstream consequences.

A low-cost proposal may reflect efficiency. It may also reflect scope narrowed in ways the sponsor doesn't fully understand; studies excluded, analytical methods not included and untested platform assumptions.

This is where the distinction between large-firm advisory and hands-on sponsor-side support matters most. A recommendation to "select a CDMO with platform fit" is not the same as reviewing every SOW line, pressure-testing scope against the specific capsid, and identifying gaps that will cost months if missed. Early-stage teams need the latter, from someone who understands their stage and budget, not a firm designed for mid- and late-stage biotech.

What I look for:

Platform fit. Has this CDMO run a similar capsid? What modifications were needed? What flexibility exists between PD and GMP? How do they handle capsids that deviate from their standard process?

Scope clarity. What's actually in the proposal? What's excluded? How are overruns handled? I have reviewed SOWs where critical PD studies were scoped out and would have needed to be added back at significant cost once the team was already committed.

Licensing and lock-in. Are the terms limiting the sponsor's ability to move the program later? I have reviewed SOWs where licensing terms would have locked sponsors into partnerships they couldn't exit, buried in contracting language, only visible when the team needed to pivot.

GMP translation. Will the PD process translate into GMP? On one program, PD completed successfully but several process areas couldn't be accommodated in GMP as-is, this was only apparent during facility fit assessment, not during PD itself.

A recent example: I supported a pre-seed/seed virtual team (early academic spinout) through CDMO selection. They needed flexibility (the academic group was still involved and iterating), small-scale RUO material fast (ruling out CDMOs with minimum scales that would generate unnecessary material at unnecessary cost), and adaptable analytics and process packages that would allow RUO-to-PD portability. Using a vetted network and a targeted RFP process, we matched them to the right partner in under one month. A process that typically takes teams without this experience three to four months of false starts.

I've built this network of CDMOs, raw material suppliers and enabling technology partners, to match programs to partners based on stage, flexibility, cost structure, and technical capability. The value is understanding that companies at different stages need different things, so knowing who specializes or is great with scale vs. agility and small scale productions that scale, help in being able to move fast while getting material you can use.

Building the IND Along the Way

One practice I now build into every engagement: maintaining a continuous production history from the earliest development runs forward, rather than assembling IND documentation retrospectively.

Most teams treat documentation as a downstream activity; something assembled after development is "done." In practice, this means details are lost, batch records are incomplete, process evolution is poorly tracked, and the Module 3 narrative gets built from bits of records and institutional memory. For programs with multiple candidates, multiple GOI configurations, and iterative process changes, this becomes a significant IND risk.

How I built this on the AFTX 201 program:

We were simultaneously developing processes for four capsid options with two GOI configurations. I built a living production history mapping every production; PD, engineering, tox, GMP, cross-referenced to the full analytical data set. This tracked process evolution across capsid-agnostic and capsid-specific operations, justified the minimal-but-sufficient process history for the IND, and allowed development reports and batch history narratives to be drafted continuously rather than reconstructed after the fact.

When it came time to assemble the Module 3, documentation was in a good place. Process descriptions, development reports, specifications, stability summaries all in a place that could be fed into the eCTD format. That contributed directly to an IND accepted with no CMC comments.

The documentation backlog problem. And why it's more common than people admit:

This doesn't only affect pre-IND programs. I recently supported an AAV company gearing up for PPQ and moving toward BLA. They had accumulated a significant backlog of documentation and reports that needed drafting, development reports, characterization reports, process history. People had left, institutional knowledge had walked out the door, and documents had fallen by the wayside. By the time they needed this material to support their PPQ campaign and regulatory filings, there were gaps that could have led to reviewer comments and held up progression.

Because I've done this work hands-on (not just reviewed it), I was able to identify open gaps and several risk factors that could be de-risked with targeted experiments before their PPQ campaign was complete. That's a different level of engagement than a reviewer flagging issues after the fact.

This kind of documentation debt is extremely common in the gene therapy space. Teams are moving fast, resources are stretched, people transition, and technical documentation doesn't keep pace with development activity. It's even more common when you don't have someone driving the work being performed at a CDMO. Reports being generated, procedures being used, process decisions being made; I've worked with a Series A company where most of these documents were either not fully complete or not generated at all. All of this was needed before a GMP run that was scheduled in 3 months.

When it's time to file an IND or assemble the documentation supporting your PPQ process, you need help from someone who understands both the science and the regulatory narrative. We've done this for teams at pre-IND through process characterization and PPQ and the earlier you start, the cleaner the path.

CDMOs provide batch records and certificates of analysis. They do not build your CMC narrative, track your process evolution across candidates, or write your IND. Having someone who does this in real time embedded in the program is one of the simplest ways to de-risk the regulatory timeline.

Ex-US Pathways: A Strategic Accelerant, Not a Shortcut

For developers where the next financing depends on clinical proof-of-concept, ex-US regulatory pathways can meaningfully accelerate FIH timelines. The most common approach: conduct an investigator-initiated trial (IIT) in a jurisdiction with a streamlined regulatory framework, then bridge that clinical data back into a US IND.

Australia's Clinical Trial Notification (CTN) scheme is frequently cited and for good reason. The abbreviated regulatory pathway offers limited pre-trial review, and the R&D Tax Incentive provides up to 43.5% back on eligible R&D expenditures for companies under $20M AUD turnover. Other jurisdictions offer their own advantages in speed, cost, and infrastructure.

But the path can be complex:

IIT-to-IND bridging. FIH data generated through an IIT is valuable, but the product used to generate it must ultimately support a US IND (if that is the end goal). Product quality, manufacturing process, documentation, and analytical characterization all need to be conducted with US IND requirements in mind even under a different regulatory framework. Teams that treat the IIT as an isolated event and plan to "figure out the bridge later" often find that their material, data, or documentation doesn't meet the bar for US filing.

Manufacturing location and quality standards. Where clinical material is manufactured, and to what standards, matters for bridging. Material produced for an ex-US IIT must be manufactured in a way that either directly supports or can be credibly bridged to a US IND submission.

Documentation and regulatory strategy. The CMC narrative must serve both the IIT jurisdiction and the eventual US filing from the start. Building this in from the beginning is far less expensive than trying to reconstruct it later.

Partner selection. Teams must work with regulatory, clinical, and manufacturing support partners who understand bridging requirements across both jurisdictions. Getting this wrong means generating clinical data or manufacturing material that can't support the US filing.

This is an active area of my practice. I am currently supporting a cross-border AAV program a Series A company manufacturing ex-US, with Phase 1 material production underway and a US IND bridging strategy navigating multi-jurisdictional regulatory, manufacturing, and quality considerations.

I've also built partnerships with ex-US vendors that maintain a US presence de-risking the manufacturing of material overseas while preserving the ability to file an IND in the US. This kind of network infrastructure matters because partner selection for ex-US programs is not just about cost and speed it's about ensuring the entire chain, from manufacturing through documentation through regulatory filing, is designed with the US bridge in view from day one.

The ex-US pathway is a powerful strategic tool when used with planning and the right support infrastructure. Without that, it can generate data and material that looks like progress but doesn't actually advance the US program.

Platform Leveraging: Accelerating Multi-Candidate Development

For developers advancing multiple candidates on the same capsid backbone increasingly common in ecosystems built around shared capsid platforms there is a significant opportunity to compress development timelines by leveraging process knowledge across programs.

The key is mapping which unit operations are capsid-agnostic (transferable across candidates sharing the same capsid) versus capsid-specific (GOI-dependent, expression-dependent, or quality-profile-dependent). When this mapping is done deliberately during the first candidate's development, subsequent candidates don't require full-cycle PD they require focused work only on the elements that change.

How I've built this in practice:

On the AFTX 201 program, I designed the process architecture for platform leverage from the start mapping capsid-agnostic versus capsid-specific operations across the entire process during the first candidate's development. When subsequent candidates entered development on the same backbone, PD focused only on capsid-specific elements: GOI-dependent expression differences, yield impacts, and quality attribute shifts. Platform elements upstream process, core purification train, formulation approach, analytical framework, and tech transfer documentation carried forward.

The result: what would have been a four-month PD cycle per candidate compressed to approximately six weeks. The analytical framework carried over with minor qualification work. Tech transfer documentation was reusable with targeted changes.

This requires deliberate sponsor-side decisions during the first candidate. It also requires understanding at the unit operation level which elements are truly capsid-agnostic and which are not. GOI can affect productivity, packaging efficiency, stability, and downstream behavior even when the capsid backbone is identical.

For developers entering ecosystems where multiple teams share the same capsid platform, this approach has direct applicability. Understanding the ability to leverage existing platform knowledge when using a common capsid can

save months of development time per candidate and having someone who has built this architecture before is what makes it actionable rather than theoretical.

Making Better Decisions Earlier

The challenges in this paper CDMO selection traps, documentation debt, ex-US pathway complexity, and the opportunity for platform leverage are all fundamentally decision-making problems. They don't require more execution. They require better early judgment from someone who understands the landscape, the tradeoffs, and which options actually fit the program, the stage, the budget, and the timeline.

Early gene therapy teams are lean by design, strong science, urgent timelines, limited runway. CMC often doesn't receive senior attention until the program is already committed to decisions that are expensive to reverse. It's the structural reality of how early companies are built and funded.

For teams entering capsid partnership ecosystems working with next-generation engineered capsids and navigating the path from capsid access to clinic the decisions you make in the next three to six months will define your timeline, your cost, and your regulatory readiness. Making those decisions with experienced sponsor-side support is how you protect the scientific advantage you've built.

This is ViroSpark.

We are the CMC and TechOps bridge for early gene therapy teams particularly those working with novel engineered capsids. We are not a giant consulting shop. We are practical operators who, de-risk the program and hand back a clean plan that keeps milestones on track. We work inside the SOWs, the batch records, and the facility fit assessments as well as the high-level strategy decks. We bring a former CTO and senior analytical sciences specialist as needed for a plug-in TechOps team when needed.

We are built for pre-commercial budgets accessible to the teams that need experienced CMC guidance the most but have historically been priced out of getting it.

ViroSpark BioConsulting Sponsor-side CMC strategy and execution support for early gene therapy programs moving from discovery to FIH/IND.

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