

CAPITAL LIGHT SCALE-UP *Utopia or Perfect Storm?*

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Capital light scale-up utilizes existing fermentation facilities, in lieu of purpose-built demonstration facilities, to bring advanced technologies to market faster and with less capital burn. It is a great plan if it can be executed, but risk comes in the form of limited options, making it far from a predictable pathway. While record funding for organism development companies has generated an impressive backlog of technologies in early-stage commercialization, the diminishing landscape of contract manufacturing organizations (CMOs) is setting up a potential perfect storm of demand significantly exceeding supply. The capital light approach can be utopia, but also can end up as a perfect storm if a venture is not prepared for the challenge ahead. The following outlines some key considerations to ensure capital light scale-up can become a reality.

Pick realism over optimism – Optimism is abundant within advanced biotechnology and it has the beneficial effect of keeping many of us in the fight, through a long and at times, challenging journey. The downside of optimism is when evaluating capital light scale-up with CMOs, whose total cost of the program is driven primarily by how long the operations will take to reach required goals. If funding is based on optimistic assumptions that do not materialize during scale-up, it places the venture in a very difficult and undesirable position of running out of resources to reach commercial viability.

Economics 101 – The economic downturn of 2008 impacted all industries, including contract manufacturing. Little new capacity has come online since then, at the same time many existing CMOs ceased operations or converted to captive use. The demand by advanced biotechnology diminished during the same period, while most ventures retrenched into development mode. The recent surge in funding and organism-focused companies has produced a significant pipeline of industrial biotechnology processes, all beginning the march to commercial operation. This suggests a future of demand exceeding supply, but at this point, it is only a forecast. The streamlined capital approach to scale-up will become a mirage to many, if forecasts are met.

Chicken or the Egg – the classic quandary of which could have come first. Even if confident of the coming surge, it is hard to raise capital to expand CMO capacity as the need is only forecasted. Personal experience has shown, non-binding partnership letters will only go so far and usually will not secure large-scale project financing. This sets the advanced biotechnology industry up for big game of “chicken” on who will pull the trigger to expand capacity. As we all learned as kids, the hardest part of playing chicken, is knowing if you need to flinch.

See the whole chessboard – Limiting your scale-up options to existing CMOs is the most defined pathway, but also the most crowded. The larger the scale and longer the need of operations, the wider to cast your net during the search. Idled facilities, brownfield sites and manufacturing facilities with underutilized assets can be a viable, although more complicated option. Looking back at the industrial biotechnologies that have successfully scaled-up over the last 15 years,

many used fermentation facilities that were not considered traditional CMOs at the time and show a pathway that needs to be seriously considered.

Apples and Oranges – the process of evaluating CMO scale-up options is a complex exercise comparing facilities with different capacities, costs and capital investments. The primary driving factor is fermenter size and efficiency, which dictates the capacity. Most CMO's have robust fermentation with limited changes required. Downstream recovery is another story, where some facilities will have more of the required equipment than others, compelling rental equipment or equipment purchase. This will generate a cost structure with CMO manufacturing fees, third party rental costs and purchase of equipment, for options with different levels of production. Depending on whether the results are viewed as average \$/kg of product or total cash burn for the effort, may generate different decisions from the analysis.

Time is not on your side – for large scale industrial fermentation (50,000 liter fermenters or larger), it can commonly take 6 months minimum to select a site, negotiate a contractual agreement, transfer the technology and do preliminary small-scale runs to be in a position to run batches in a large-scale fermenter. If the CMO requires additional equipment or the business arrangement is more complex than standard fee for service (equity, incentives, etc.), the timing can extend to 12 months or longer. Ventures that have a promising organism and potential product do not want to be the one standing when the music stops. Companies relying on CMOs for product commercialization should start early to ensure they meet public commitments.

For additional details on the complexities of capital light scale-up, check out my previous publications [Contract Fermentation Landscape](#) and [Scaling-up Through Contract Manufacturing](#).

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