Challenges of Scale-up and Commercialization

Why the project manager model may represent the best outsourcing option

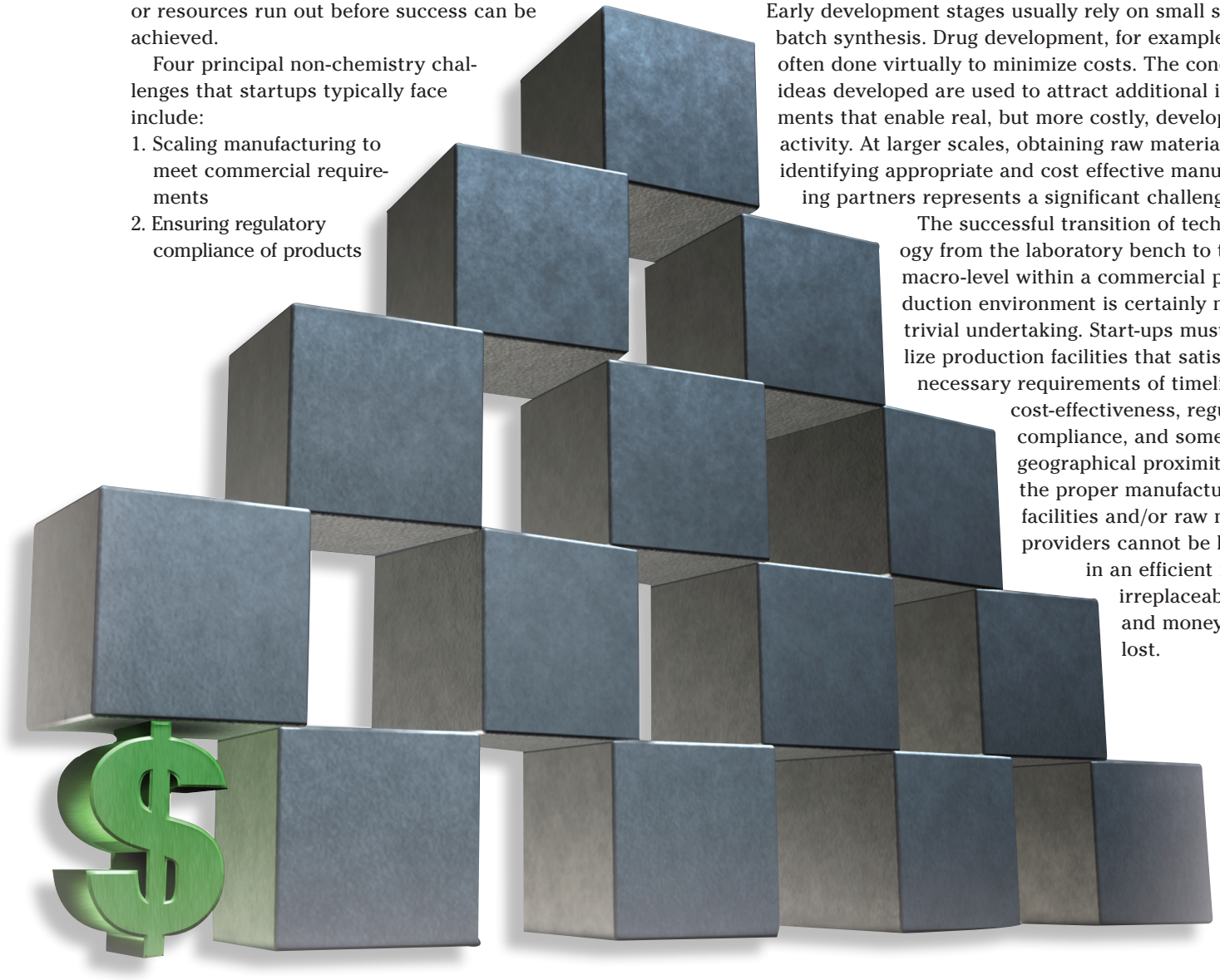
By Christopher Kulp, Executive Vice President, Richman Chemical

The development of new chemistry-based products for life science markets requires the expertise of talented researchers. However, these same researchers are typically not prepared to solve the many other critical problems necessary for successful commercialization. Without the requisite expertise in scale up and commercialization, many early-stage companies find that competitors beat them to the market or resources run out before success can be achieved.

Four principal non-chemistry challenges that startups typically face include:

1. Scaling manufacturing to meet commercial requirements
2. Ensuring regulatory compliance of products
3. Securing adequate funding for product development and manufacturing
4. Protecting intellectual property

We will discuss these challenges and review a number of solutions.



SCALING MANUFACTURING TO MEET COMMERCIAL REQUIREMENTS

Early development stages usually rely on small scale batch synthesis. Drug development, for example, is often done virtually to minimize costs. The conceptual ideas developed are used to attract additional investments that enable real, but more costly, development activity. At larger scales, obtaining raw materials and identifying appropriate and cost effective manufacturing partners represents a significant challenge.

The successful transition of technology from the laboratory bench to the macro-level within a commercial production environment is certainly not a trivial undertaking. Start-ups must utilize production facilities that satisfy the necessary requirements of timeliness, cost-effectiveness, regulatory compliance, and sometimes geographical proximity. If the proper manufacturing facilities and/or raw material providers cannot be located in an efficient manner, irreplaceable time and money are lost.

ENSURING REGULATORY COMPLIANCE

Drugs and other products manufactured for human consumption must comply with governmental or industry-specific regulations. For pharmaceuticals, it is the current Good Manufacturing Practices (cGMP) of the FDA. Food grade and kosher regulations may apply to food and nutritional products.

During the R&D phase, companies can minimize expenditures by producing test quantities using non-compliant batch production methods. However, converting these processes to meet regulatory requirements for scaled-up commercial production can be extremely time-consuming and costly. Frequently a change in facilities is also needed, further complicating matters.

In the production of pharmaceutical products, cGMP regulations, for example, require that all commercially produced drugs and pharmaceutical products meet stringent assay, quality, and purity requirements. Facilities must have appropriate quality management systems in place that can detect, investigate, and correct product quality deviations. Investigational new drug (IND) submissions to the FDA can easily be delayed and rejected by insufficient data, inadequate reporting or insufficient cGMP reference standards. This may necessitate rapid preparation of clinical trial batches and validation and/or production of GMP-grade material to serve as a reference standard itself.

Even if the custom compound is the active pharmaceutical ingredient (API), and therefore does not require cGMP certification, the supply of specialized intermediates and precursors for life science applications may necessitate specific ISO certification on the commercial scale. This is becoming increasingly relevant as medical device companies request custom synthesis services for new excipients and components for novel drug-device combinations.

SECURING ADEQUATE FUNDING FOR PRODUCT DEVELOPMENT AND MANUFACTURING

While there are many potential sources of funding for product development, obtaining funding is nonetheless highly competitive, and each investor or funding organization will have different requirements. Funding sources include venture capital (VC) groups, angel investor consortiums, and grant opportunities such as Small Business Innovation Research (SBIR) available through governmental agencies such as the National Institutes of Health. Identifying the proper grant options for the technology in question, as well as employing experts with grant-writing expertise, is of paramount importance. It is vital for start-up organizations to "get in front" of VC and angel boards to make a pitch for their novel technologies. External vendors and partners with existing relationships with such funding organizations are attractive options for young companies in need of capital.

In addition, companies can also license their technology to commercial partners with synergistic or complementary technologies. Big Pharma typically leverage their resources in this way to bolster R&D pipelines. In order to do this, however, proof-of-concept work, data collection, and analysis must be conducted to convince potential investors to fund its product development activities. This is often one of the most expensive and difficult steps in the life of a start-up. While these fledgling companies typically confirm the bioactivity of a drug candidate on their own, the ability to prepare a comprehensive technical package suitable for licensing or transfer often remains beyond their internal capabilities. Thus, it is important for these outfits to identify external resources capable of handling synthesis, testing, and formulation work at all scales.

PROTECTING INTELLECTUAL PROPERTY

Companies must balance the need to avoid any patent infringements or protect their own intellectual property (IP), and safely share their confidential process information with development partners. IP should be cross-referenced against existing patents and then protected during development and technology transfer. While this is typically conducted internally by legal staff or through a contracted external law firm, any perceived gaps may need to be addressed through additional laboratory work. For instance, a start-up may need to prepare additional patent example compounds, quickly synthesize competitive samples, perform analytical mea-

surements for confirmation of substantive differences/similarities of target compounds, or identify trace contaminants and elucidate impurity profiles. A start-up needs this work performed expeditiously to maximize future income within their limited patent life.

SOLUTIONS

The objective of any start-up is to commercialize its technology in the shortest amount of time and as cost-effectively as possible. Any lost time is irreplaceable as a start-up risks burning through existing funds. Even if successful, the time to profit under patent protection increases with each minute the technology remains non-commercial. As mentioned, researchers and investors typically have little experience in effectively or efficiently identifying, vetting and managing production facilities (national/international); sourcing raw materials; or locating specialized equipment and instrumentation. More importantly, this is not their core competency, and they usually lack the in-house resources to do all of this. Since time is of the essence, a hit or miss approach is not strategic. Instead, the optimal approach may be to outsource commercialization requirements to experienced specialists.

The most strategic reasons to outsource are cost and time. Most companies would not outsource if it were more expensive than doing the same work in house. The key drivers for this cost differential, which can be regarded as the underlying reasons for outsourcing, are access to production capacity and facilities, access to expertise (regulatory, scale-up, etc), reduced investment in capital assets and fixed costs, access to reasonably priced raw material supplies, and the ability to stay focused on core competencies.

The advantages to outsourcing far outweigh any perceived disadvantages. In order to mitigate any loss of control over functions, it is important to ensure corporate cultures mesh, processes are transparent, communication is open, and performance objectives are closely monitored.

OUTSOURCING MODELS

There are various outsourcing models which can be utilized depending on specific need, company philosophy, and/or time and financial constraints. We review several major ones below.

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VENDOR COMPETITOR MODEL

In this model, multiple vendors with similar capabilities compete for business. Vendor selection is generally based on time and cost, although cost is frequently the overriding factor. Many start ups think multiple vendors will drive costs down. Usually the opposite applies. Many potentially good vendors drop out of bid requests that have too many participants. When they perceive poor odds of winning the bid, they do not want to waste time and money preparing one. Even the successful bidder may not be the best choice if their low cost comes with inadequate support and incentive to properly support the project.

PRE-QUALIFIED VENDOR SELECTION MODEL

Many companies maintain extensive data on past and present suppliers, with details of capabilities and performance levels. Companies may use an outsourcing department to assure an appropriate match for a particular project can be made with regard to a potential supplier's capabilities, past performance, and business model. If not on record, this information can also be generated on a case by case basis for evaluation purposes. Most pharmaceutical companies pre-qualify potential suppliers and set up preferred provider relationships, pre-defining outsourcing strategies for particular areas within the company. This model typically works well, but it is costly in terms of manpower and economic expenditures. From a practical standpoint, the theoretical payoff is usually not compatible with existing financial and timing constraints.

PARTNERSHIP MODEL

A company may choose to partner with one specific vendor for certain aspects of product manufacture. Usually, this is a contractual relationship, and the risk is shared so that outcome is equally important to both parties. The vendor who participates in this type of business relationship has a keen interest in seeing the project through to a successful conclusion, and payment is at least partially contingent on a successful outcome. While this strategy can be very successful, it is severely limiting in terms of scope, capabilities, and frequently, capacity. Ideal partners for one stage of the product development process may not be optimal for later stages of the outsourcing process. Furthermore, external factors affecting one of the partners in a negative manner will often affect the partnership as a whole.

PRINCIPAL VENDOR MODEL

The company uses one principal outsourcing vendor with the understanding that vendor will be further outsourcing parts of the project to others. The principal vendor is still the supplier of record and is the responsible party for due diligence and compliance with regulations. This is a somewhat complex arrangement, and it effectively places all outsourcing requirements (contracted and sub-contracted) into the hands of personnel who may be inexperienced with project management arrangements involving third parties. Significant attention is allotted to the principal contract work and sub-contracted efforts may suffer due to a lack of experience and/or an absence of long-term client-vendor relationships.

PROJECT MANAGEMENT MODEL

In this model, a firm hires a company to provide project management services for the project being outsourced. The Project Manager (PM) does not conduct the actual physical manufacturing within their own facilities. Instead, the PM provides access to a specialized network of suppliers with whom it maintains established relationships. Enlisting the services of a PM effec-

tively expands the potential sources for any company engaging in outsourcing. The PM provides industry vendors, such as contract research organizations (CROs) or contract manufacturing organizations (CMOs), with technical competencies, scope of capabilities, track record, business culture, available equipment, manufacturing capacity, scalability, and reliability. A PM is assigned to the client in need to handle its specific requirements. The PM functions as the client's de facto outsourcing department--but without the internal cost.

A competent PM should provide extensive technical and manufacturing experience leading to compressed timelines, lower costs and increased technical capabilities. This allows for improved focus on new technology development and sales/marketing efforts. Furthermore, PMs can facilitate the provision of auxiliary services as needed, including product development, raw material sourcing, and logistics coordination and regulatory support.

Within the parameters of the Project Management model, the outsourcing client is significantly dependent upon the expertise of the PM to provide compatible service offerings. However, the model itself is based upon a cooperative, risk-sharing foundation between the client and the PM. It is not uncommon to invoice for services rendered only after the project has been successfully completed.

CONCLUSION

The proliferation of start-up firms within the life sciences market highlights the need for competent, highly skilled vendor partners capable of handling custom chemistry projects. Effective outsourcing to CROs/CMOs provides a significant opportunity to accelerate product development, maintain operating budgets, and use internal resources effectively- for the life science industry as a whole. A wider acceptance of the benefits of such a relationship can only be gained by fostering a greater understanding of the outsourcing process. Start-up organizations may find that, in many cases, the Project Management Model offers the most benefits when it comes to successfully commercializing technology within the shortest amount of time. ■

ABOUT THE AUTHOR:

Christopher Kulp serves as Executive Vice President at Richman Chemical. He has years of experience in development and manufacturing within the pharmaceutical and chemical industries, and has four U.S. patents and two European patents to his credit. He has contributed to successful commercialization efforts in the areas of natural and synthetic polymers, organometallics, and pharmaceuticals. Chris has an M.S. from Stevens Institute of Technology and an MBA from Temple University.

ABOUT RICHMAN CHEMICAL

Richman Chemical, Inc. provides custom chemical synthesis, custom manufacturing, and raw material sourcing in the life sciences, specialty chemical, biotechnology, pharmaceutical and emerging technology industries. Founded in 1988 by Ed Richman, the company is headquartered outside of Philadelphia. For more information visit www.richmanchemical.com.