Catering to a Growing Demand for Small-Volume Parenteral Manufacturing

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Tags: | *CDMO* | *Injectables* | *Orphan Drugs* | *Grifols* | *Parenteral Manufacturing* |

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Oriol has been working in pharmaceutical marketing and sales, with a focus on the hospital business both domestic and internationally, for 30+ years. He has spent the last 15 years devoted to the strategic business growth of products and markets. In the past 10 years, he has concentrated on the development of the contract manufacturing business unit at Grifols, designing the strategy of positioning and communication, as well as driving the company towards necessities of the market.

Drug candidates are becoming increasingly complex as manufacturers continue to focus on niche and personalized medicines. Contract development and manufacturing organizations with process and capacity flexibility, and wide-ranging expertise in small-volume GMP manufacturing are needed to support efforts by pharma companies to rapidly bring these specialized products to the market.

Expanding Orphan Drug Market

The global market for drugs that are designed to treat rare diseases and receive "orphan" drug designation is expected to expand at a healthy compound annual growth rate of 11% from 2018 to 2026, reaching a value of $262 billion, according to EvaluatePharma.[1] That growth rate is nearly double the rate for the overall pharma market, and by 2024 orphan drugs will account for 20% of worldwide prescription sales.

A recent study revealed that orphan drugs comprise more than 40% of all innovative pharmaceuticals that have expanded the human drug target landscape from 1983 to 2017.[2] At the time of the report (June 2018), of 803 drug candidates in clinical trials, 40% targeted rare diseases. In addition, over the last several years, orphan drugs have accounted for more than 40% of newly approved molecular entities,[2] and in 2017 half of the 42 new active substances launched in the United States were orphan drugs.[3]

In 2018, the U.S. FDA granted the highest number of new drug approvals ever — a total of 59 NMEs as of December 27th – more than half of which were for rare diseases.[4] Similarly, the European Medicines Agency approved many more drug products in 2018 — 45 compared with 28 in 2017. Of those approvals, the number with orphan drug designations doubled from the previous year to 17.[5]

There is no indication that this trend is slowing down. In 2017, the FDA approved 80 new orphan indications, with 57 approved in the first eight months of 2018. That same year, 429 unique drugs under development were granted orphan designations by the FDA.[3] Clearly, many of the drugs being developed today are intended to treat rare diseases and a fair amount are developed using genomic information to provide targeted therapies that address genetic mutations or malfunctions.

Growing Interest in Small Molecule Injectables

The injectable drug market is expanding in large part because of the rise of biologic drugs, which generally must be administered by injection or infusion. The demand for small molecule parenteral products is also increasing.[6]

According to Transparency Market Research, the global small molecule injectable drugs market will expand substantially from 2017 to 2025 due to growth in generic injectables, which is outpacing that of innovator drugs, a strong pipeline of small molecule injectable drugs and significant investment in R&D for small molecules.[6]

Challenges of Small-Volume Manufacturing

The focus on the development of drugs to treat rare diseases and the growing interest in formulating small molecule APIs as injectable products is creating challenges for many pharmaceutical companies and their outsourcing partners. Manufacturing of smaller volumes of products must still be compliant with cGMP regulations, but at smaller scale and generally with much higher value materials and under accelerated timelines. Newer targeted therapies are often more chemically complex and can present analytical challenges. Minimizing the quantity of material required for testing is essential given the high value of many orphan drugs.

Important Role for CDMOs

Despite the growth of biologics, small molecules continue to dominate the pharmaceutical market, both with respect to existing (branded and generic) and developmental drug products. Notably, large pharma companies tend to outsource more activities related to their small molecule products than they do biologics.

In addition, most small and emerging pharmaceutical companies, which are significant drivers of small molecule orphan drug development, lack the resources, personnel and process development, and regulatory expertise required to efficiently advance drug candidates through the full development and commercialization process. These companies rely heavily on contract service providers to implement their process and formulation development, validation, regulatory compliance and manufacturing activities. It is particularly important for pharmaceutical companies developing small molecule injectable products to work with a CDMO partner that has the expertise needed to rapidly develop robust, high-quality manufacturing processes that are readily scalable.

Quality Underlies All Activities

Indeed, the first concern of any CDMO should be safety and compliance during manufacturing. Effective CDMOs must have demonstrated histories of performing the appropriate stability, compatibility, extractable/leachable and sterility studies to

ensure the optimum safety and performance of sterile drug products, whether packaged in premixed bags or vials. It is also essential that the CDMO has a well-established culture of quality and effective quality systems in place.

Grifols' commitment to quality includes ongoing investments in automation technologies such as "Form-Fill-Seal" technology (developed by Grifols Engineering) for the production of ready-to-use, premixed polypropylene bags and fully automated glass vial filling lines designed to minimize human interactions with drug products. Artificial vision systems (developed in collaboration with Grifols Diagnostic) enable the automatic inspection of injectable products for particulates. Our commitment to quality is also reflected in our approval for parametric release of parenteral solutions, which facilitates reduced timelines for product release, allowing our clients to get their products to the clinic and market more quickly.

Flexibility and Experience a Must

CDMOs must have a combination of flexibility and wide-ranging expertise to manage multiple, varied projects with many different customers simultaneously. Flexibility and experience are needed to support pharma companies developing small molecule injectable drugs with orphan and accelerated approval designations within dramatically shortened timelines. Flexible capacity is also necessary if CDMOs wish to support projects as they move from the clinic to commercialization.

Orphan drugs designed to treat small patient populations may not necessarily be produced in very small annual volumes.7 Some of these drugs are taken daily and administered in high doses. Therefore, it is important for CDMOs to have strategic capacity planning capabilities in order to ensure that the right capacity is available at the right time. The key is to offer a range of services, capacities and specialized technologies to support customers as their projects move through the development cycle.7

Grifols welcomes orphan/rare disease drug projects at the clinic to commercial stage. We have the ability to produce low numbers of units (i.e. 100,000) in premixed bags or vials and can expand production to millions of units if or when volume demand increases. If needed — and with the commitment of our customers — Grifols is willing to invest in additional production lines as projects successfully move from the clinic to the market.

Small Business with Big Pharma Backing

As a business unit within a global pharmaceutical manufacturer, Grifols Partnership has access to financial, technical, regulatory and other resources not readily available to standalone CDMOs, yet we are flexible enough to be an ideal partner for small and emerging pharma companies. Our operators use the same equipment for both internal and external projects and, therefore, have extensive experience using these systems.

Notably, the equipment in our plants is designed specifically for Grifols by Grifols Engineering. This vertical integration fits with Grifols' quality culture; it enables us to control the entire process, ensuring the highest quality. We also have a collaborative and integrated project management strategy, bringing together cross-functional teams with representatives from manufacturing, R&D, quality assurance, quality control, regulatory and sales and marketing to support our clients. With a collaborative effort, built upon strong internal relationships, we provide the highest

standards of quality to our customers while helping to reduce or prevent potential problems that could result in unwanted delays in delivery of products to market.

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